Brain development in Chinese children and adolescents: a structural MRI study

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This is the first systematic study of Chinese children's brain development. Using optimized voxel-based morphometry, we investigated age-related changes in gray and white matter in Chinese children and adolescents aged 7 to 23 years. Results showed mostly linear reductions, but also some linear increases, in gray matter in many regions of the brain. Gray matter changes were more evident in the parietal and temporal regions than in the frontal and occipital regions. White matter showed significant linear increases in internal capsule, arcuate fasciculus, superior and inferior longitudinal fasciculus, and cingulate fasciculus. *NeuroReport* 18:875–880 © 2007 Lippincott Williams & Wilkins.

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Introduction

Recent advances in MRI technologies and analytical methodologies have made it possible to investigate human brain development *in vivo*. These studies have documented a general pattern of children's and adolescents' brain development. During childhood and adolescence, there are reductions in overall gray matter volume and increases in overall white matter volume [1–3]. These changes, however, show regional heterogeneity. For example, phylogenetically older, lower-order areas (sensorimotor regions, occipital regions) mature earlier than newer, higher-order association areas (upper and lower parietal lobes, prefrontal cortex) [4]. Previous studies also show that the changes of white matter are linear, but those of gray matter tend to be nonlinear in some regions (a prepubertal increase and a postpubertal decrease in the frontal and parietal regions) [3–6].

Although these and other related studies have helped us to understand the general patterns of brain development, their findings are nonetheless limited to a particular group of people: Caucasians. Little is known about brain development among other racial/ethnic groups [7,8]. On the one hand, brain development should follow some universal patterns because of the shared evolutionary history of all human groups. On the other, it may show group variations. Indeed, certain differences in brain volumes and shapes among adults of different racial/ethnic groups have been documented [9–11]. Kochunov *et al.* [10] detected brain shape differences in several gyri in the frontal, temporal, and parietal lobes between English-speaking Caucasians and Chinese-speaking Asians. Such differences may have resulted from complex interactions between numerous genetic and environmental factors. Given the plastic nature of the brain and the existing differences in social/cultural environments for children of different racial/ethnic groups, it is likely that brain development may not follow exactly the same pattern for different groups.

It is imperative to document brain development in many groups and to compare their patterns. Using voxel-based morphometry, this study systematically examined the brain developmental patterns of Chinese children and adolescents. Voxel-based morphometry is objective and fully automated for detecting differences in regional concentration or volume of brain tissue composition [12]. It has been used to evaluate brain morphometrical differences in different populations [13,14].

Materials and methods

Participants

We recruited 158 normally developing right-handed Chinese children and adolescents (78 males and 80 females) between the ages of 7.26 and 22.80 years (mean age = 15.03, SD = 4.70 years). Male and female were almost evenly distributed (either 50–50 or a difference of one child) for every year of age. Participants were recruited as part of several cognitive studies. They were screened for neurologic disorders and any history of learning disability or developmental delay. Written informed consent was obtained from all participants, and in the case of those younger than 18 years of age, from their parents as well.

MRI acquisition

All participants were scanned on a 2 T prestige scanner (Elscint/GE, Haifa). Brain structural MRIs were acquired by using a T1-weighted GR sequence (TR = 25 ms, TE = 6 ms, flip angle = 28°, FOV = 220 × 220 mm^2, matrix size = 220 × 220 mm, voxel size = 1 × 1 × 2 mm^3). A qualified pediatric neuroradiologist read all the scans and found no abnormalities.

Creation of customized brain templates

As pediatric brains are different in size, shape, and tissue composition from adult brains [15], the use of the adult brain default template in the computer package SPM (SPM2, Wellcome Department of Cognitive Neurology, London, UK) is likely to result in distortions. Therefore, customized brain templates were created from all participants included in this study. Using 12-parameter affine linear transformation for maximally preserving most brain regional characteristics in children, all participants' images were spatially normalized to the same stereotactic space, followed by segmentation into gray matter, white matter, and cerebrospinal fluid using the technique reported in [12,16]. Voxel intensities in the segmented images represent probabilities of being a particular tissue type. To create customized brain templates, we averaged across participants affine-only transformed images and the segmented gray matter, white matter, and cerebrospinal fluid images, respectively. These four images were then smoothed with an 8 mm full width at half maximum isotropic Gaussian kernel.

Optimized voxel-based morphometry

The protocol of optimized voxel-based morphometry [13] involves (a) segmenting the original structural MRIs into partitions of gray matter, white matter, and cerebrospinal fluid in their native space with customized brain templates; (b) spatially normalizing individual gray matter image to customized gray matter prior; (c) reapplying normalization parameters to normalize the original MRIs into the customized template space; (d) segmenting again the normalized MRIs into compositions of gray matter, white matter, and cerebrospinal fluid; (e) modulating the brain tissue component using the Jacobian determinant to correct for volume changes introduced during spatial transformation; and (f) smoothing the segmented modulated images with an 8 mm full width at half maximum isotropic Gaussian kernel.

Statistical analysis

Statistical analyses for global volumes were performed using SPSS 11.5 (Chicago, Illinois, USA). We examined both linear and quadratic effects of age on total gray matter, white matter, and intracranial volumes. Significance level was set at $P < 0.05$.

Voxel-based analyses were carried out using SPM2 to assess associations between age and gray/white matter volumes with intracranial volume as a covariate. Specifically, F test was used to determine whether the developmental curves of gray/white matter were linear or quadratic (that is, whether the coefficients for the linear and the quadratic terms were significantly different from

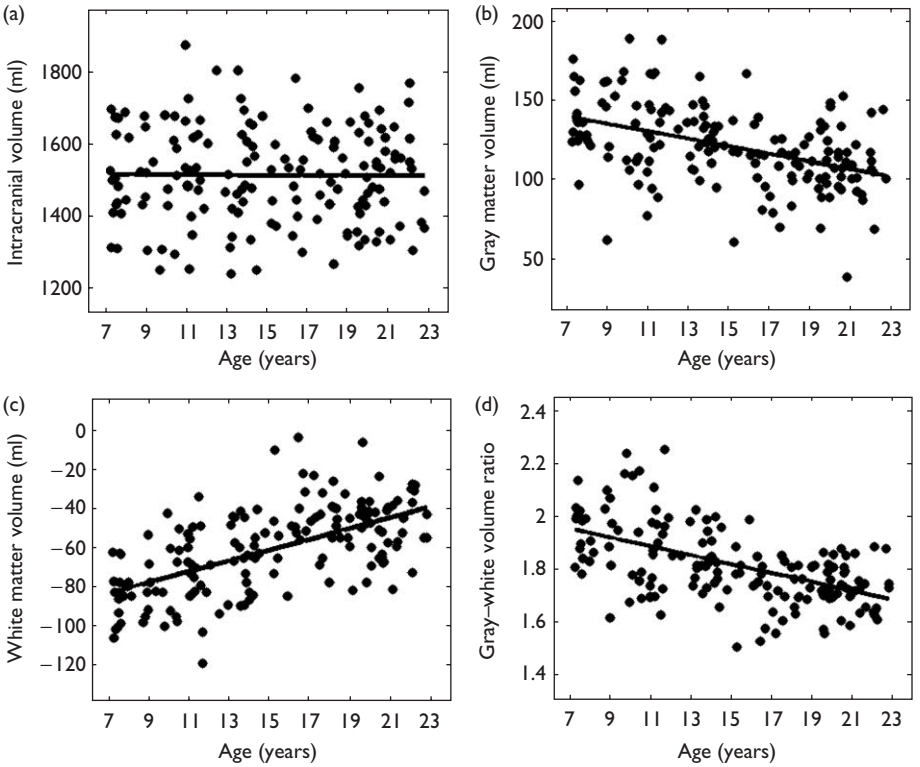

Fig. 1 Scatter plot of global effects of age for 158 participants: intracranial volume, gray matter volume (corrected for intracranial volume), white matter volume (corrected for intracranial volume), and gray–white matter volume ratio. The fitted linear regression lines are superimposed.

zero). For a linear trend, post-hoc *t*-test was used to determine whether the correlations between age and gray/white matter volume were positive or negative. Significance level for these analyses was set at $P<0.05$, corrected for multiple comparisons using family-wise error (FWE).

Results

As shown in Fig. 1a, intracranial volume did not change significantly with age, overall $R^2<0.001$, $F(1,156)=0.013$, $P=0.909$. Controlling for intracranial volume, global gray matter volume decreased linearly with age (Fig. 1b), overall $R^2=0.877$, $F(2,155)=554.164$, $P<0.001$, with a significant linear coefficient, $T=-6.082$, $P<0.001$. Global white matter volume increased linearly with age (Fig. 1c), overall $R^2=0.875$, $F(2,155)=541.477$, $P<0.001$, with a significant linear coefficient, $T=9.318$, $P<0.001$. Consequently, the gray–white matter volume ratio decreased linearly with age (Fig. 1d), overall $R^2=0.311$, $F(1,156)=70.392$, $P<0.001$, with a significant linear coefficient, $T=-8.390$, $P<0.001$. The quadratic coefficients in all cases failed to reach significance (all Ps >0.148).

In terms of regional variations in the effects of age, Table 1 shows brain regions, corrected *P*, *T* scores, and the stereotactic coordinates for gray matter that showed linear effects of age. Positive correlations between regional gray matter volume and age were observed in the bilateral hippocampus, amygdala, inferior temporal gyrus, and left fusiform gyrus (Fig. 2 and Table 1). In contrast, many brain regions showed significant age-related reductions in gray matter volume (Fig. 3 and Table 1). The most significant change was in bilateral parietal lobe (Fig. 3). Fewer changes were found in the frontal lobe. All regional effects were linear, with the exception of the bilateral posterior cingulate that displayed a curvilinear trend (a steep decline between ages 7 and 13 and leveling off afterward).

In terms of white matter, there were no significant age-related decreases. Instead, there were significant age-related linear increases in internal capsule, arcuate fasciculus, superior and inferior longitudinal fasciculus, and cingulate fasciculus (Fig. 4).

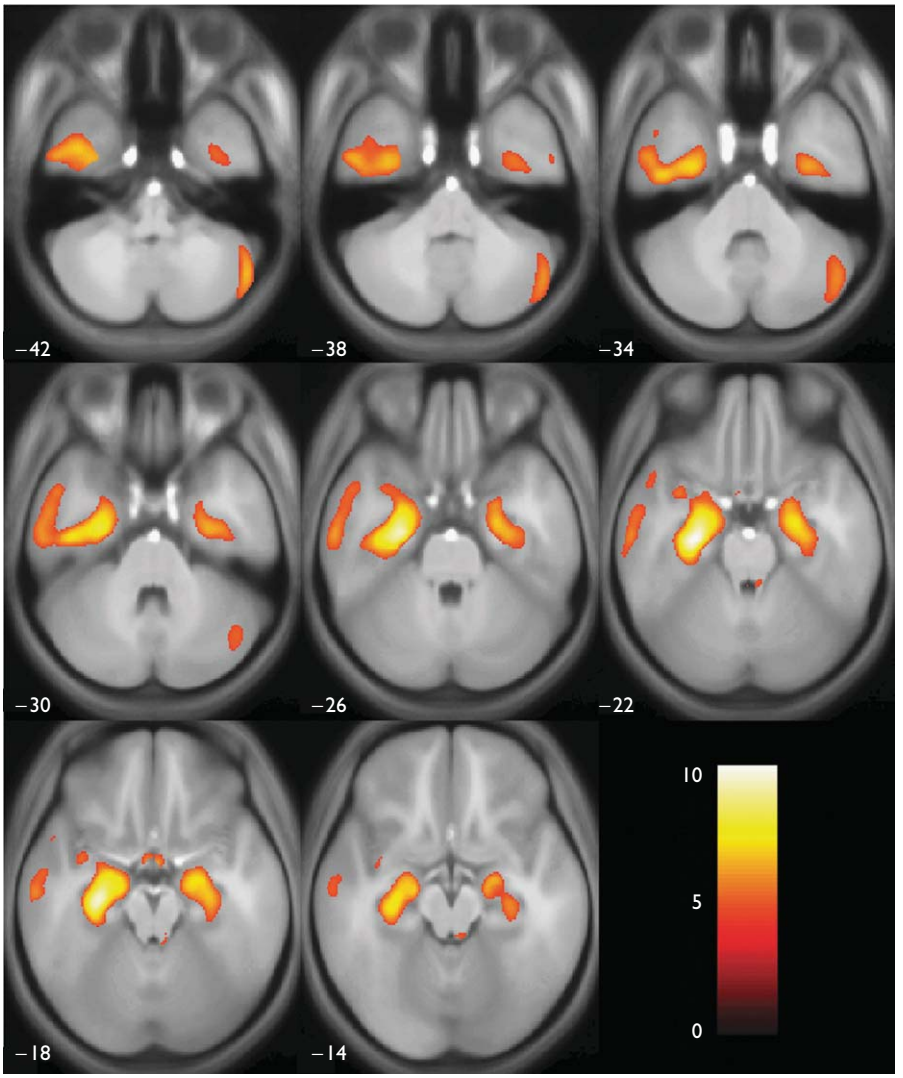

Fig. 2 Significance maps of positive correlation of gray matter volume with age.

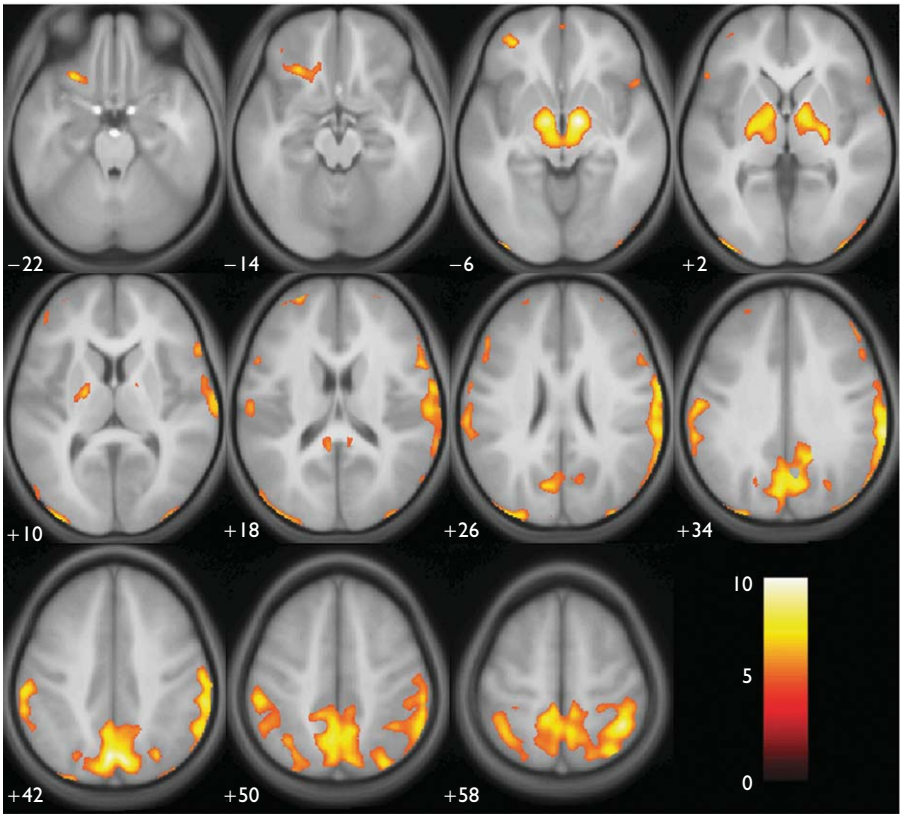

Fig. 3 Significance maps of negative correlation of gray matter volume with age.

Table 1 Gray matter volume: correlation with age ($P < 0.05$, corrected using FWE)

Brain regions	*P*	*T*	Peak coordinates		
Gray matter volume: positive correlation					
L hippocampus	0.000	10.90	−27	−16	−19
R hippocampus	0.000	6.74	27	−16	−19
L amygdala	0.000	9.19	−25	−9	−16
R amygdala	0.000	8.05	25	−9	−16
L inferior temporal gyrus	0.000	7.11	−33	−6	−35
R inferior temporal gyrus	0.014	5.34	52	−6	−33
L fusiform gyrus	0.000	7.98	−40	−16	−24
Gray matter volume: negative correlation					
L Precuneus	0.000	10.03	−3	−69	41
R Precuneus	0.000	9.77	7	−70	40
L inferior parietal lobule	0.000	6.19	−58	−35	42
R inferior parietal lobule	0.000	9.33	65	−32	29
L superior parietal lobule	0.000	7.48	−35	−58	53
R superior parietal lobule	0.000	7.83	33	−61	59
L inferior frontal gyrus	0.000	8.08	−29	25	−18
R inferior frontal gyrus	0.000	6.88	57	13	16
L middle frontal gyrus	0.000	6.82	−28	60	9
R middle frontal gyrus	0.000	7.72	28	63	9
L superior frontal gyrus	0.000	6.95	−28	63	0
R superior frontal gyrus	0.001	5.93	28	61	2
R superior temporal gyrus	0.012	5.37	66	2	3

FWE, family-wise error; L, left; R, right.

Discussion

To our knowledge, this is the first systematic study on brain development of Chinese children. In this section, we discuss the general patterns of Chinese children's brain development and make some tentative comparisons with those found in previous research on children of other countries.

First, the global effects of age found in this study are consistent with previous volumetric studies such as those of the US children [1–3]. An overall reduction in gray matter volume and an overall increase in white matter volume was found between childhood and adolescence. All age-related global changes for our Chinese sample were, however, linear, which is consistent with several previous studies [1,2], but no two other studies that reported nonlinear developmental patterns of gray matter (peaking around puberty) for the US children [3,4]. Further research is needed to investigate the reasons for such different findings.

Second, our results showed more significant age-related reductions in gray matter volume in the parietal lobe than in other lobes (Fig. 3). This is consistent with the results for children of other countries [4,6]. Reductions in gray matter volume in the parietal lobe correspond to improvements of basic cognitive functions typically associated with the parietal lobe (visuospatial function, reasoning, attention, skill learning, and arithmetic processing).

Third, the development of temporal lobe was relatively complex, showing both positive and negative age-related changes in gray matter volume (for example, increases in bilateral inferior temporal gyrus and reductions in right superior temporal gyrus). Gogtay *et al.* [4] also noted a complex pattern of development of the temporal lobe, albeit somewhat different from ours. One common finding across various studies, including ours, is the positive age-related changes in hippocampus [17], an important

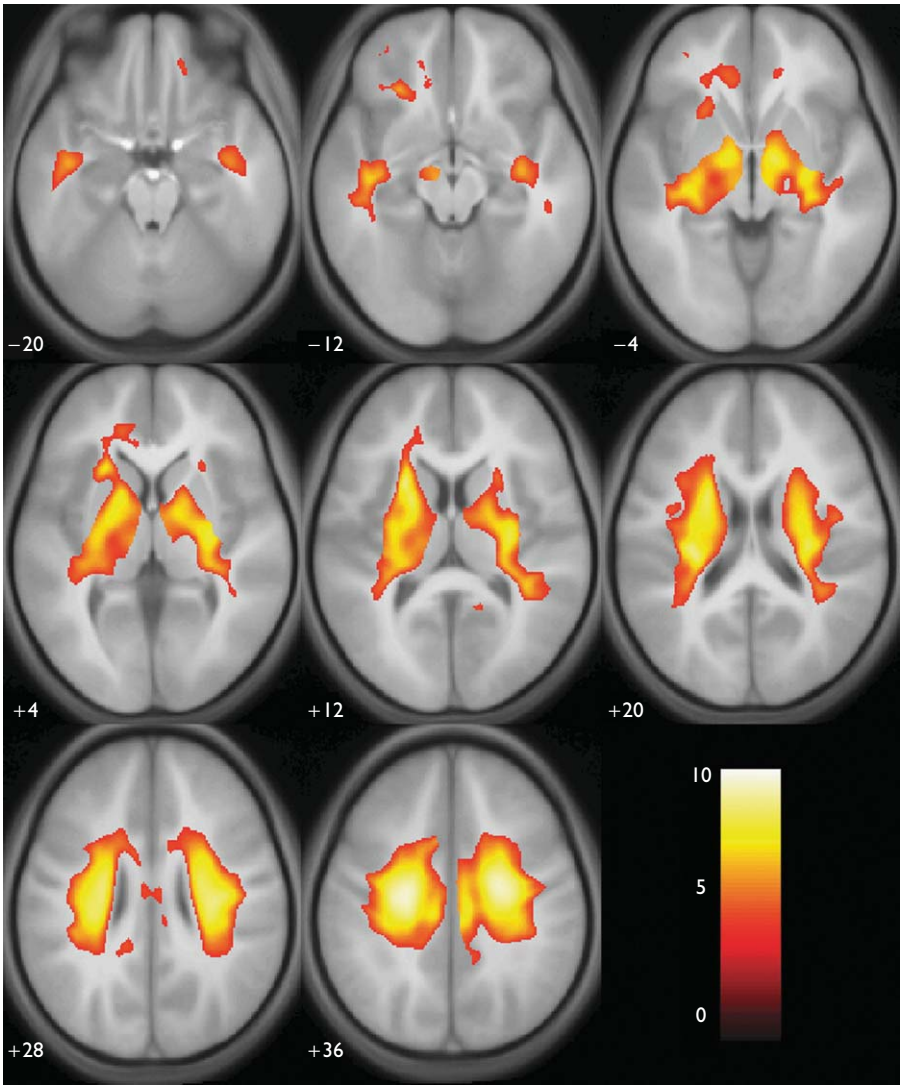

Fig. 4 Significance maps of positive correlation of white matter volume with age. Note that from Figs 2 to 4, all *Ps* < 0.05, corrected for multiple comparisons using family-wise error. The parametric map of the *t* statistic (SPM_t) is superimposed on the customized brain template from all participants (left of the plane is the left of the brain). The color bar represents the *T* score.

region for memory. This positive change is presumably responsible for the remarkable increase in memory capacity from ages 4 to 18 years. Similarly, both neuroimaging and neuropathologic studies have demonstrated that gray matter reduction in hippocampus is associated with memory deficits [18].

Fourth, the frontal lobe also showed some significant changes. They appeared to be fewer than those indicated by previous research [4,6], but without direct comparisons, it is uncertain whether the rate of changes differed significantly between our Chinese sample and other samples.

Finally, our data showed age-related linear increases in white matter in several brain regions. The changes in internal capsule and arcuate fasciculus found in our study are consistent with previous findings from a Canadian study [5]. Different from Paus *et al.* [5] study, however, we also found notable age-related increases in white matter volume in three other areas: cingulate fasciculus, superior and inferior longitudinal fasciculus (Fig. 4). At the moment it is not clear why these areas showed significant changes for Chinese children, but not for Canadian children.

Conclusion

In this study, we investigated changes in gray matter and white matter to provide a comprehensive picture of brain development among Chinese children and adolescents. Our results confirmed the overall similarity in general patterns of brain development between Chinese children and their counterparts in other countries. Indications, however, exist that several patterns of brain development may be different across different groups. Further research is needed to test directly such differences and to explain them if they are confirmed.

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