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Research article

Examining population differences in cerebral morphometry between Chinese and Indian undergraduate students

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HIGHLIGHTS

- We use brain MR images to exam the morphometric differences between Chinese and Indian undergraduate students.
- ROIs of GM volume, cortical thickness, and cortical surface area are utilized simultaneously to reveal the brain structure on different levels.
- Group-related and gender-related brain structure differences between Chinese and Indian undergraduate students are found in this study.

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ABSTRACT

The aim of this study is to examine potential population differences in brain morphometry using magnetic resonance imaging (MRI). Thirty-six Chinese and thirty-two Indian undergraduate students are included in this study. All images are processed using BrainLab toolbox to obtain the morphometric values of gray matter volume, cortical thickness, and cortical surface area in each region of interest (ROI). We use ROI-based analysis to investigate ethnic differences using the three types of measurements. Cerebral variations of the brain between Chinese and Indian groups are mostly distributed in the frontal lobe, temporal lobe, and occipital lobe. Subgroup analysis reveals sex differences between the two groups. Our study demonstrates population-related differences in brain morphometry (gray matter volume, cortical thickness, and cortical surface area) between Chinese and Indian undergraduates.

1. Introduction

Study of population differences has attracted attentions in recent years [1]. Magnetic resonance imaging (MRI) is a common tool for non-invasive study of anatomy in the human brain. Having population-specific MRI is especially important to investigate the differences in the brain structure.

Preliminary studies examining brain structure differences have been reported across adults from different populations. Because positioning or selection of a region of interest (ROI) is an essential step for the quantification of brain images, ROI-based analysis is widely used on brain MR images [2,3]. Differences in ROIs have been found between Chinese and Caucasian cohorts [4]. MRI analysis shows volumetric differences of specific regions in the cerebellum, amygdala, and orbital frontal cortex between the African-Americans and Caucasians [5]. Differences in frontal lobe, temporal cortical regions, basal ganglia, and midbrain are found between Chinese and Caucasians [6]. Moreover, fMRI study indicates that brain structural differences between Oriental-Koreans and Caucasian-Americans in the fusiform are detected [7]. These findings indicate that brain structures vary from population to population.

Based on these studies, we put forward a hypothesis that there are brain structural differences between the two groups of young adults in East Asian. In the study, we present a ROI-based method to research on brain structures between Chinese and Indian undergraduate students. The aim of this study is to investigate the brain

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morphometric differences in the Asian community, which may provide pilot evidence for revealing cerebral differences of young people between the two populations.

2. Methods

2.1. Participants

Thirty-six Chinese undergraduates (aged 21–26, mean age 21.9 years, 22 males and 14 females) and thirty-two Indian undergraduates (aged 21–26, mean age 22.1 years, 19 males and 13 females) from Soochow University are included in this study. All subjects are right-handed and normal or corrected to normal vision. Each participant is surveyed a structured clinical interview to rule out any psychiatric or neurological diagnoses. None of them has previously received any kind of stimulant or medications. They are also requested to abstain from caffeine or other substances that can influence on activity levels of MRI scanning. After task completion, all subjects are financially reimbursed and given small gifts. The study is approved by the Ethics Committee of the Third Affiliated Hospital of Soochow University. Written informed consents are obtained from all subjects.

2.2. MRI acquisition

Brain MRI are performed with a 3-T Siemens scanner equipped with a standard head coil with the following parameters: repetition time (TR) = 2300 ms, echo time (TE) = 2.98 ms, flip angle (FA) = 90°, field of view (FoV) = $256 \times 256\,\text{mm}^2$.

2.3. Image processing

All structural brain MR images are processed using BrainLab [8] (Fig. 1) with automatically generated parameters. Original images are reoriented and resampled to a standard format to normalize the orientations, voxel sizes, and volume sizes. N3 bias field correction is performed to remove the intensity inhomogeneity. Then, a deformable-surface-based brain extraction algorithm is used to remove non-brain tissues from the preprocessed images. A level-sets-based tissue segmentation algorithm is used to separate GM, WM, and cerebrospinal fluid (CSF) by constraining the cortical thickness within a biologically reasonable range with 1–6.5 mm [9–11]. After that, the brains are nonlinearly registered to the template. And then we warp the map of pre-labeled ROIs in the template onto the subjects. Accurate reconstructions of inner, central and outer cortical surfaces are achieved by a deformable surface method. Although we obtain 90 volumetric ROIs [12], only 78 cortical ROIs are used ignoring 12 subcortical regions [13]. Considering individual differences, gray matter volume of each ROI is normalized by dividing the total brain volume, and the cortical surface area of each ROI is normalized by dividing the total surface area of the brain. Because the accuracy of registration and segmentation may affect the precision of the morphometric measurements, all image processing algorithms in the toolbox are already published in leading journals [14–17] and show improved accuracy and effectiveness compared with similar algorithms.

2.4. Statistical analysis

Subject characteristics are described in Table 1. Student's *t* test and *chi-square* test are conducted on age and gender respectively. The significance level of the *p* value is set as 0.05. Bonferroni correction is employed for multiple comparison. The significance level for individual test is determined at 0.05 divided by the number of ROIs examined (78 ROIs). The statistical analysis is performed using SPSS 20 (SPSS Inc., Chicago, IL, USA).

3. Results

Age and gender distributions are similar for the two groups. Age and sex are well matched in each group. Differences of GM volume, cortical thickness, and surface area are examined between the two groups (Fig. 2). In Table 2, results show that significant population differences are found in seventeen ROIs. Fourteen of these measurements are numerically higher for the Chinese population, including two ROIs in GM volume (the left superior frontal gyrus and right precuneus), four ROIs in cortical thickness (the bilateral inferior frontal gyrus (triangular), right temporal pole (superior), and right lingual gyrus), and nine ROIs in cortical surface area (the left orbitofrontal cortex (superior), left middle frontal gyrus, right orbitofrontal cortex (inferior), right middle occipital gyrus, right Heschl gyrus, right temporal pole (superior), left middle temporal gyrus, and left inferior temporal gyrus). Three of the measurements are higher for Indian population, including two ROIs in GM volumes (the right orbitofrontal cortex (inferior) and right inferior frontal gyrus (triangular)) and one ROI in cortical thickness (right orbitofrontal cortex (inferior)). Scatterplots of the GM volume, cortical thickness, and cortical surface area in these ROIs are shown in Figs. 2–4. .

For each gender, we conduct subgroup analysis with twenty-two Chinese male students and nineteen Indian male students in the male subgroup and fourteen Chinese female students and thirteen Indian female students in the female subgroup (Table 2). In the male subgroup, five ROIs are higher for Chinese males, including one in GM volume (right orbitofrontal cortex (superior)), three in cortical thickness (right inferior frontal gyrus (triangular), left orbitofrontal cortex (inferior), right lingual gyrus), and one in cortical surface area (right Heschl gyrus), and two ROIs are higher for Indian males, including one in GM volume (right inferior frontal gyrus (triangular)) and one in cortical thickness (right orbitofrontal cortex (inferior)). In the female subgroup, eight ROIs are higher for Chinese females, including one in GM volume (left superior frontal gyrus (dorsal)), two in cortical thickness (left orbitofrontal cortex (inferior) and left calcarine cortex), and five in cortical surface area (right precentral gyrus, right Insula, left fusiform gyrus, left middle temporal gyrus, and left inferior temporal gyrus), and two ROIs are higher for Indian females, including one in GM volume (right orbitofrontal cortex (inferior)) and one in cortical thickness (right orbitofrontal cortex (inferior)). These ROIs in group analysis and subgroup analysis remain significant even after multiple comparison correction (Bonferroni corrected $p < 0.0001$). The ROIs in comparison between the two populations are not identical to the ROIs in subgroup comparison. There are five ROIs show statistically significant on sex differences, which are not detected in the two populations.

4. Discussion

As a pilot study, we investigate the population differences of the brain between Chinese and Indian students using structural MR images. We hypothesize that there are brain structural differences between the two East Asian groups. According to the experimental results, region-specific anatomical variations of the brain are distributed in the frontal lobe, temporal lobe, and occipital lobe between the two groups, which validates our hypothesis. ROI based method is used to explore our ethnic data. Because ROIs are defined on the basis of brain function in specific regions, it is useful to analyze brain structure in areas of interest rather than to discern across the whole brain. Previous imaging morphometric studies focus on

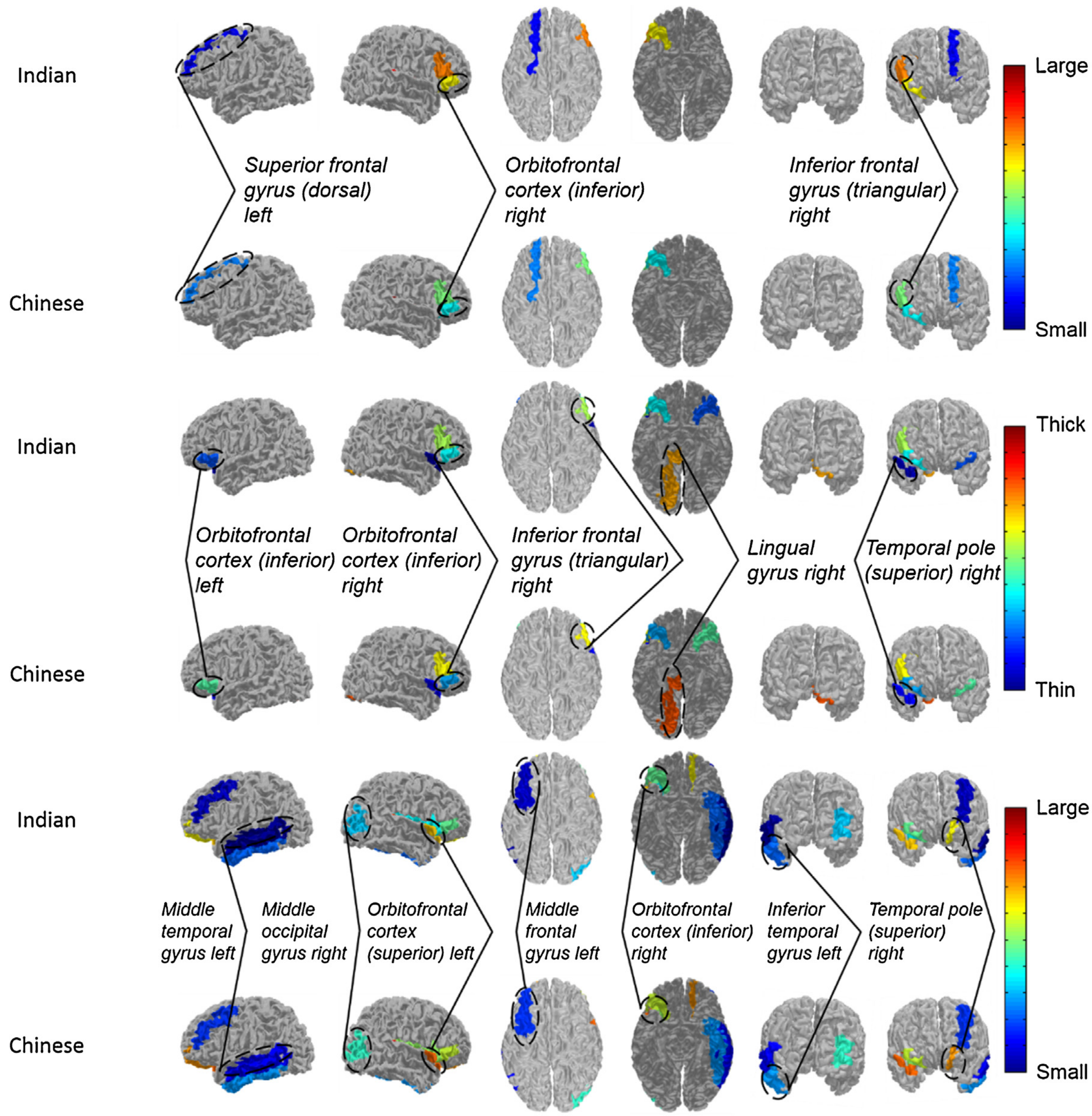

Fig. 1. ROIs with statistically significant differences on GM volume (the first two rows), cortical thickness (the middle two rows), and cortical surface area (the last two rows) are illustrated.

Table 1
Subject characteristics are listed. There are no significant differences between the two groups in gender and age.

		Chinese ($N = 36$)	India ($N = 32$)	Total ($N = 68$)	Statistics	p value
Gender	Male	22 (61.11%)	19 (59.38%)	41 (60.29%)	chi-sq = −0.14	0.8860
	Female	14 (38.89%)	13 (40.62%)	27 (39.71%)		
Age range		21–26	21–26	21–26	–	–
Age		21.90 ± 1.17	22.10 ± 1.35	22.21 ± 1.32	t = −1.5	0.14

brain volumes, which is unable to detect the possible cortical structure. In this study, we are able to perform the volume-based and surface-based analysis of the whole brain with the state-of-the-art algorithms, which is appropriate for detecting volumetric changes (GM, WM, and CSF) and topographic variations (cortical thickness and cortical surface area).

Volumetric analysis shows region-specific differences inter-populations [18,19]. In our study, GM differences between Chinese and Indian groups are found in the frontal lobe and parietal lobe, which indicates that differences may affect the ability of information processing, physical activity, motor speech, and emotions regulation.

Cortex is regarded as the highest achievement of biological evolution and the foundation of the ability of human thinking [20], which is responsible for higher mental functions. In our study, cortical thickness differences are mainly in the frontal lobe, occipital lobe, and limbic lobe between the two groups. The lingual gyrus is one of the statistical significant ROIs in occipital lobe. Therefore, cortical variations will lead to differences in logical analysis and visual memory.

Table 2
ROIs with statistically significant changes in GM volume, cortical thickness, and surface area between overall comparison and subgroup comparison are listed. The GM volume and cortical surface area of each ROI are normalized over the whole brain.

ROI	Chinese (N = 36) Mean (SD)	Indian (N = 32) Mean (SD)	Chinese male (N = 22) Mean (SD)	Indian male (N = 19) Mean (SD)	Chinese female (N = 14) Mean (SD)	Indian female (N = 13) Mean (SD)	p values
Gray matter volume							
Superior frontal gyrus (dorsal) left	0.0080 (0.0004)	0.0078 (0.0005)	–	–	0.0088 (0.0003)	0.0081 (0.0002)	<0.0001
orbitofrontal cortex (superior) right	–	–	0.0033 (0.0002)	0.0027 (0.0006)	–	–	
Inferior frontal gyrus (triangular) right	0.0052 (0.0006)	0.0053 (0.0005)	0.0051 (0.0006)	0.0060 (0.0005)	–	–	<0.0001
Orbitofrontal cortex (inferior) right	0.0052 (0.0005)	0.0054 (0.0006)	–	–	0.0050 (0.0004)	0.0055 (0.0006)	<0.0001
Precuneus right	0.0010 (0.0001)	0.0008 (0.0001)	–	–	–	–	<0.0001
Cortical thickness							
Inferior frontal gyrus (triangular) right	2.1278 (0.1310)	2.0281 (0.1198)	2.2898 (0.1153)	2.1037 (0.1263)	–	–	<0.0001
Orbitofrontal cortex (inferior) left	2.6840 (0.1418)	2.1316 (0.1809)	2.6476 (0.1280)	2.3712 (0.2159)	2.7333 (0.1493)	1.9021 (0.1203)	<0.0001
Orbitofrontal cortex (inferior) right	2.2616 (0.1471)	2.3095 (0.1611)	2.2168 (0.1141)	2.3066 (0.1868)	2.3102 (0.1684)	2.3125 (0.1141)	<0.0001
calcarine cortex left	–	–	–	–	2.1278 (0.0652)	1.5590 (0.0847)	
Lingual gyrus right	1.5781 (0.0920)	1.5309 (0.1149)	1.5899 (0.0899)	1.5288 (0.1123)	–	–	<0.0001
Temporal pole (superior) right	2.7944 (0.2515)	2.7204 (0.2121)	–	–	–	–	<0.0001
Cortical surface area							
precentral gyrus right	–	–	–	–	0.0214 (0.0016)	0.0206 (0.0016)	
Orbitofrontal cortex (superior) left	0.0068 (0.0007)	0.0057 (0.0010)	–	–	–	–	<0.0001
Middle frontal gyrus left	0.0300 (0.0016)	0.0260 (0.0018)	–	–	–	–	<0.0001
Orbitofrontal cortex (inferior) right	0.0110 (0.0011)	0.0093 (0.0010)	–	–	–	–	<0.0001
Insula right	–	–	–	–	0.0136 (0.0007)	0.0128 (0.0009)	
Middle occipital gyrus right	0.0156 (0.0014)	0.0134 (0.0013)	–	–	–	–	<0.0001
fusiform gyrus left	–	–	–	–	0.0161 (0.0012)	0.0150 (0.0013)	
Heschl gyrus right	0.0018 (0.0003)	0.0012 (0.0003)	0.0018 (0.0003)	0.0013 (0.0002)	–	–	<0.0001
Temporal pole (superior) right	0.0067 (0.0009)	0.0054 (0.0009)	–	–	–	–	<0.0001
Middle temporal gyrus left	0.0351 (0.0018)	0.0307 (0.0022)	–	–	0.0355 (0.0022)	0.0336 (0.0022)	<0.0001
Inferior temporal gyrus left	0.0235 (0.0020)	0.0200 (0.0022)	–	–	0.0238 (0.0022)	0.0229 (0.0021)	<0.0001

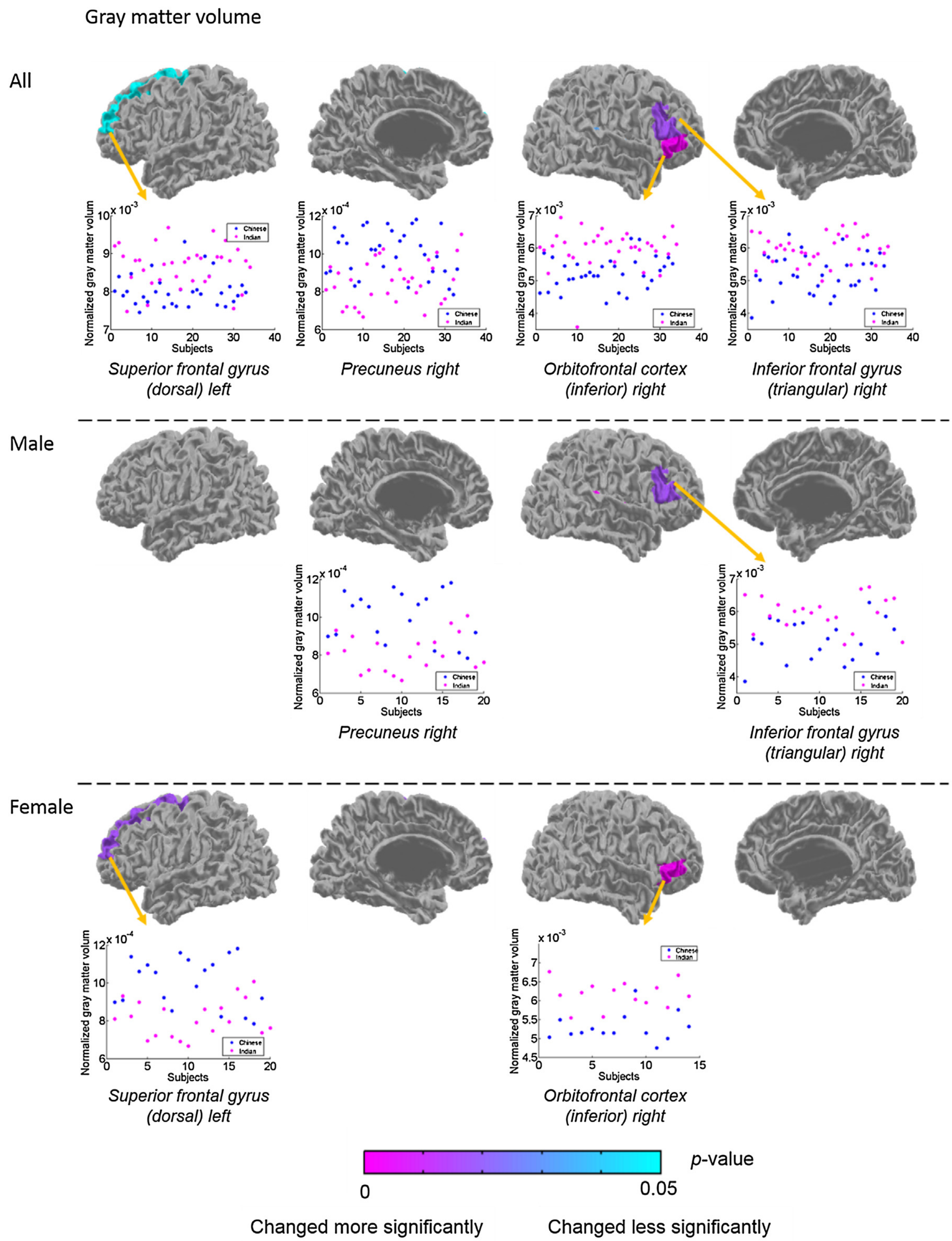

Fig. 2. *p* values and scatterplots of regional GM volume between Chinese and Indian groups are illustrated. The color bar of *p* values is provided below. Gray colors indicate non-significant regions.

Our studies find that Chinese group has larger cortical surface area in the frontal lobe, temporal lobe, occipital lobe, and limbic lobe compared with the Indian group. Few studies have investigated race-related brain structural differences on cerebral cortex. Our findings on cortical thickness and cortical surface area are the first evidences in revealing structural differences between Chinese and Indian undergraduates. Studying the cortex between the two groups will increase our understanding of population differences of the brain.

Although the GM volume, cortical thickness, and surface area are all related the GM structure, each of them conveys different information. GM volume provides information on volume, density, while cortical thickness reflects the distance between the inner surface and outer surface of the GM. In addition, cortical surface

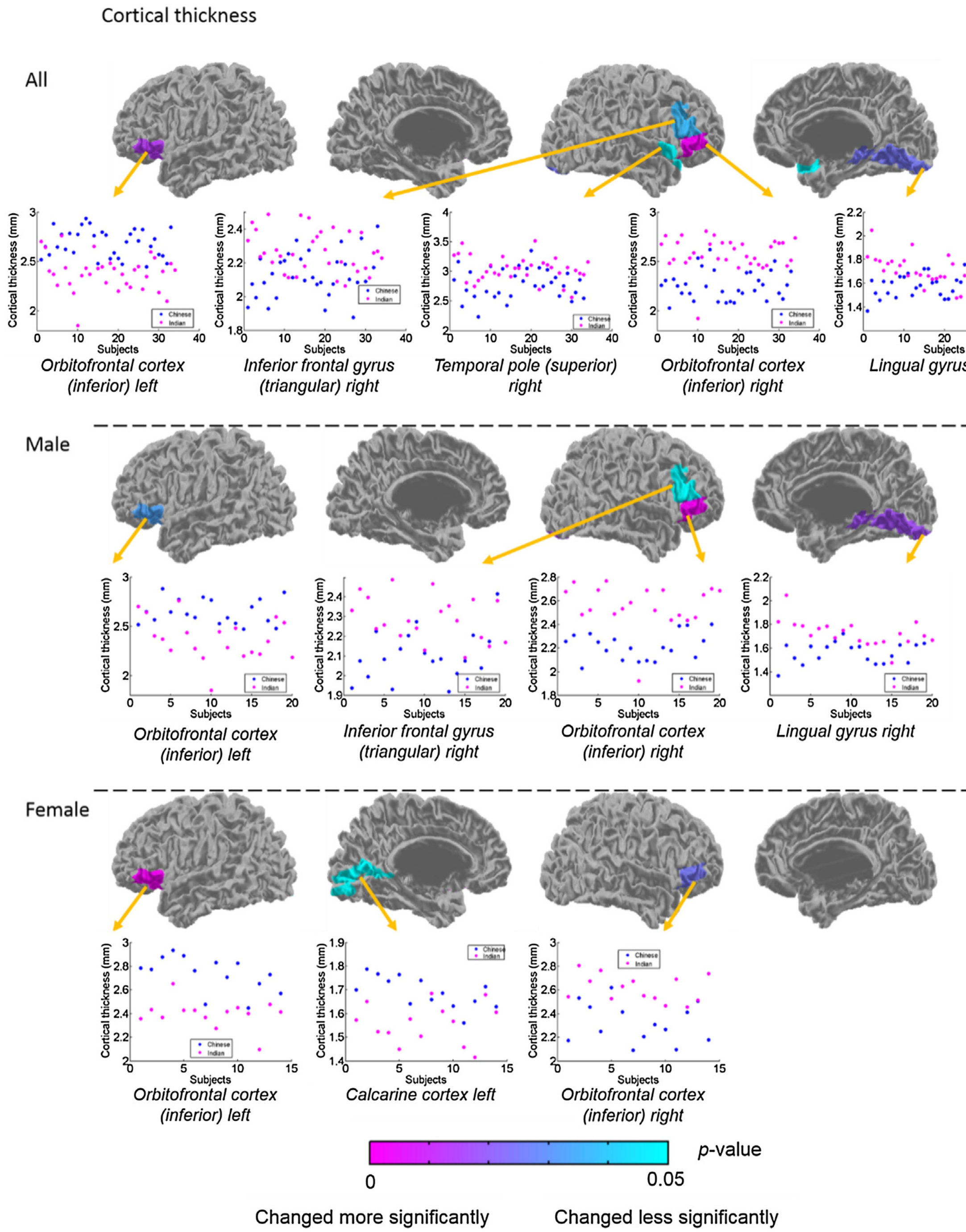

Fig. 3. *p* values and scatterplots of cortical thickness between Chinese and Indian groups are illustrated.

area shows the pattern of gyri and sulci. Moreover, the algorithm of each measurement is different, which can explain the inconsistency in our results. Analysis on the three measurements simultaneously can help reveal the group variations in different levels, which provides complementary information and helps fully describe the structure differences of the brain. Based on the structural differences, we predict that there were functional differences. Cerebral structures are highly variable among different populations, and between different genders. Therefore, in our study, subgroup analyses show sex differences on the three types of measurements. Note that the ROIs show inconsistency in overall comparison and subgroup comparison and show different variation trend in subgroup comparison even more. Although the structural differences may lead to brain functional differences, neuro structure can be affected by many different factors including neonatal and postnatal environments, life experiences, diet, cultural elements, or individual genetics. There needs large number of data to fully analyze the brain variations between the two population.

Differences in brain structure and function are associated with dissimilarities of genetics and environmental between populations. The brain structures are affected by many factors, such as customs, life styles, literature and art, system of value. Different historical geographical environments form different cultural atmosphere, which lead to differences in populations. Analysis of the morphometric measurements reveals that the GM volume, cortical thickness, and surface area are significantly different ($p < 0.0001$)

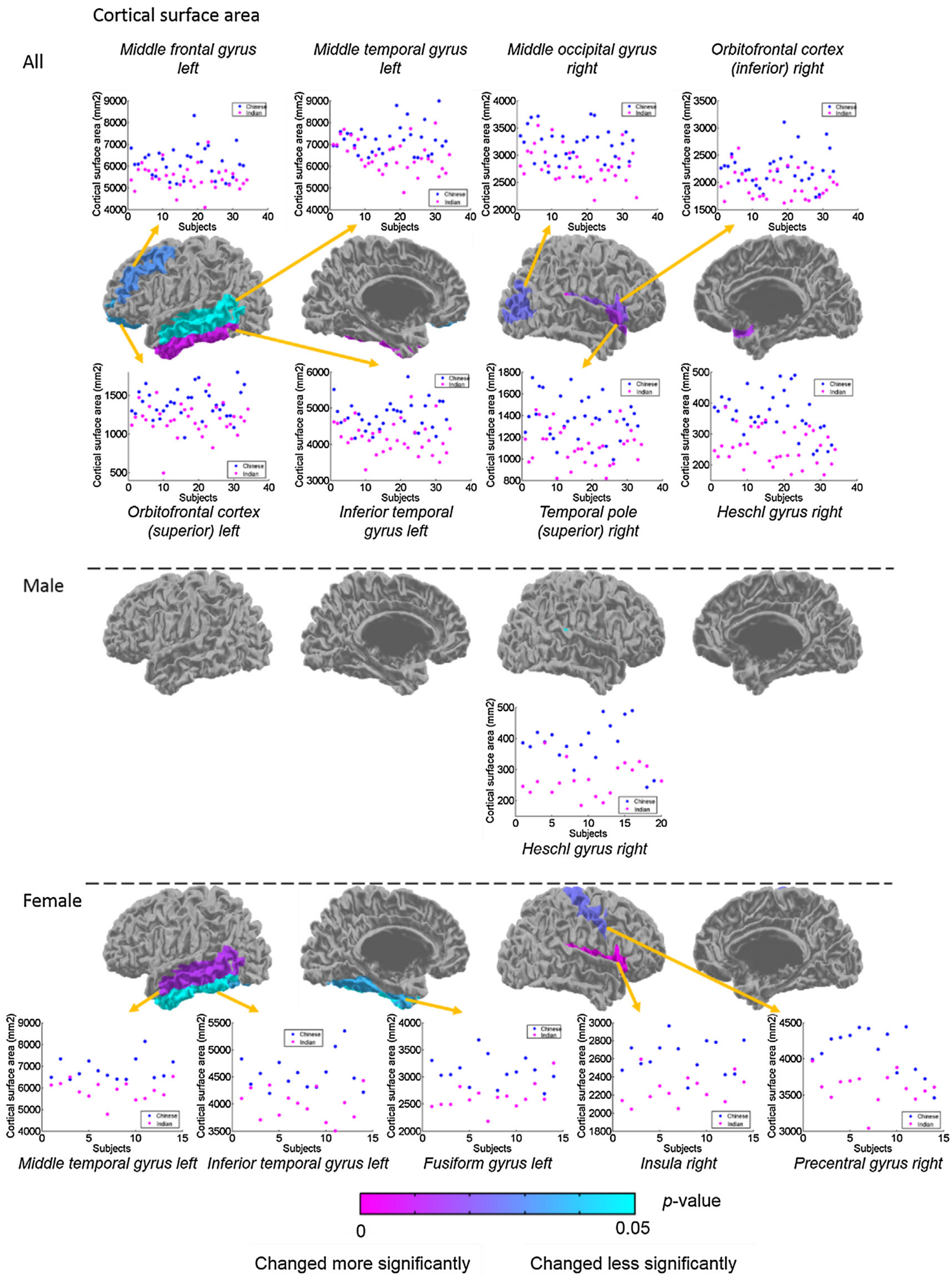

Fig. 4. *p* values and scatterplots of cortical surface area between Chinese and Indian groups are illustrated.

between the two populations. Specific reasons for the differences in brain morphometry require detailed analysis in the future.

This study has several limitations. First, as a pilot study, we just conduct the ROI-based analysis. However, studying ethnic differences of the brain is complex that needs more investigation, such as voxel-wise analysis. Second, subjects' diversity and size should be taken into account. We will conduct more sufficient and detailed experiments, which would involve more ethnicities and cover different ages as we collect more data in the future. Third, in order to better explain the sex differences, more studies are required in the future.

5. Conclusions

Our study has demonstrated population-related differences in brain morphometry between Chinese and Indian undergraduates. The population-related brain regions highlighted in our study include the frontal lobe, temporal lobe, and occipital lobe. The brain structural differences are affected by many factors, including genetics and environment. The precise role and the extent of the role of any of these factors in influencing gray matter volume, cortical thickness, or surface area need further studies.

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