31st Annual International Conference of the IEEE EMBS
Minneapolis, Minnesota, USA, September 2-6, 2009

Development of NTU Standard Chinese Brain Template: Morphologic and Functional Comparison with MNI Template using Magnetic Resonance Imaging

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Background and Purpose: The brain structure mismatch between western and eastern people may lead to an inappropriate interpretation of neurocognitive studies. To minimize this interracial misinterpretation, we developed the National Taiwan University Chinese Brain Template (NTU-CBT).
Methods: 102 (M/F=55/47) healthy Chinese subjects were recruited and received 3T MR brain scans. The template development processes were based on the construction process of Montreal Neurological Institute (MNI) template. Further pilot functional magnetic resonance imaging (fMRI) studies with blocked design visual stimulation and foot tapping task were performed on 3 volunteers and applied to both MNI template and NTU-CBT for analyses.
Results: 7 subjects were excluded due to motion artifacts. The average brain size of 95 (M/F=50/45) subjects was 16.0 cm in length, 13.9 cm in width and 11.3 cm in height, which was 88.9%, 97.9% and 84.3% of the size of MNI template, respectively. Maximum dimensional differences came from the height of superior brain and the length of posterior brain. The average activation voxel volume of the fMRI studies applying to NTU-CBT was 80.7% of that to MNI template in visual stimulation, and 72.8% in foot tapping task. Noticeable mismatches were noted between interpolating original data to NTU-CBT and MNI template.
Conclusions: Morphologic differences between MNI template and NTU-CBT do lead to spatial mismatch in functional studies, especially at cortical regions of superior and posterior brain. With the development of NTU-CBT, we look forward to more accurate interpretation in neurocognitive studies for Chinese subjects.

Keywords: Brain template, NTU-CBT, MNI template, atlas, Morphometric analysis, Functional Magnetic Resonance Imaging (fMRI).

Manuscript received April 6, 2009.

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I. INTRODUCTION

There had been a rapid growth in imaging technology over the past decades, which led to advanced understanding of human brain structures and functions. Among these imaging modalities, magnetic resonance imaging (MRI) is one of the non-invasive tools. For the purpose of population-based assessment of brain function and anatomy, standard brain template is necessary for spatial normalization of individual brain onto the standard template.

Montreal Neurologic Institute (MNI) template, a template based on MRI, was adopted by the Statistical Parametric Mapping (SPM) program and has been the most widely used for human brain mapping studies [1,2,9]. It incorporated 305 young normal controls (M/F=239/66, age 23.4±4.1 y/o) whose scans were spatially normalized into the Talairach system by linear transformation [1,2].

However, the brain structure mismatch between western and eastern people due to the diversity of environmental and genetic factors may lead to inappropriate interpretation of neurocognitive studies. The structural differences between subjects of various age, gender, and races cannot be resolved satisfactorily in the currently available standard brain templates even by nonlinear normalization approach [2].

To minimize this interracial misinterpretation, we developed the National Taiwan University Chinese Brain Template (NTU-CBT), which is an ethnic-specific anatomical and functional brain template based on brain MR images of healthy Chinese individuals. We also measured morphometric parameters and analyzed fMRI data with this novel NTU-CBT, instead of MNI template, to investigate the possible discrepancies.

II. MATERIALS AND METHODS

A. Subject Recruitment

102 healthy right-handed volunteers (M/F=55/47) without a past history of any neuropsychiatric disorder and substance abuse were recruited. 7 subjects were later excluded because of large motion artifacts or obvious structural asymmetry. 95 subjects were finally included (M/F=50/45), and the age range was 19~42 years old (mean age=25.7 y/o).

B. Data Acquisition

The MR brain images were taken with Modified Driven Equilibrium with Fourier Transform (MDEFT) gradient-echo sequence by a Bruker 3T Biospec MRI machine. The main reason to use this sequence was the ideal balance of imaging quality and scanning time. Each dataset was carefully examined to avoid illness or apparent asymmetry. The scanning parameters were determined as follows: TR=24.36 ms, TE=4.8 ms, TI=1360 ms, NEX=1, FOV=256 mm^3 to achieve full coverage of the brain, Matrix size=256 x 256 x 256, and voxel size=1 mm x 1 mm x 1 mm, a higher spatial resolution than MNI 305 template (2 mm x 2 mm x 2 mm). Total scan time was around 20 minitues for each subject.

C. Realiagnment and Transformation

To construct the template, we followed the well-established model of neurological coordinates conducted by Talairach and Touenoux [3]. This 3-D coordinate system set three orthogonal axes on the Anterior Commissure (AC)—Posterior Commissure (PC) line, Vertical Anterior Commissure (VAC) line and midline of the human brain. In our study, the axes were defined as: y-axis (anterior-posterior direction), z-axis (top-bottom direction) and x-axis (left-right direction) [4]. The construction processes were similar to that of MNI template [5]. In summary, the processes composed of realignment, transformation, registration and final average of these brain dataset. We used self-designed graphical user interface (GUI) program written by Matlab for realignment and MIPAV software (Medical Image Processing, Analysis, and Visualization) for the transformation and registration [6]. The complete processes were described as followed:

1. Each brain dataset was loaded and received 3-axis rotation of AC-PC alignment. AC of each brain dataset was placed on the same coordinate (128, 128, 128) in individual image space.
2. All AC, PC, upper limit (UL), lower limit (LL), right extent (RE), left extent (LE), anterior limit (AL), and posterior limit (PL) were manually assigned. The length of anterior brain (LAB), length of posterior brain (LPB), height of superior brain (HSB), height of inferior brain (HIB), width of left brain (WLB), width of right brain (WRB) and inter-commissural length were calculated by experienced neurologists.
3. Average brain size and scaling parameters were obtained by calculating average distances between landmarks; all datasets and summing average were equalized to derive the size of the first-pass brain template.
4. All datasets were normalized to the first-pass brain template by 9 degree of freedom (DOF) linear transformation. 9 DOF composed of translations, rotations, and scalings in x, y, and z axes.
5. Finally, all equally weighted normalized datasets were averaged to get the NTU-CBT.

D. Functional MRI experiment

3 healthy individual Chinese subjects were recruited to perform the blocked design 1 Hz foot tapping and 8 Hz checkerboard visual stimulation fMRI experiments. A 6-trial blocked design was adopted with “On-Off” persisting for 18-18 seconds. During each run, 72 volumes were obtained with a total time of 216 seconds.

A Blood Oxygen Level Dependent Echo Planar Imaging (BOLD-EPI) sequence (TR/TE=3000/30 ms) was used with FOV 240 mm x 240 mm x 140 mm and matrix size 64 x 64 x 28. The slice thickness was 5 mm without gap. Functional images were obtained from 28 slices oriented with AC-PC line, and the in-plane spatial resolution was 3.75 mm. Functional MRI data were preprocessed and analyzed with statistical parameter mapping (SPM2) software [7]. Both NTU-CBT and MNI template were applied to thereafter.

III. RESULT

The hemispheric features between Chinese males and females are shown in Table 1, whereas the cerebral dimensions of this newly developed NTU-CBT are compared with MNI 305 template in Table 2. The average Chinese brain size is 16.0 cm in length, 13.9 cm in width and 11.3 cm in height, and the average AC-PC distance is 2.53 cm. The brain dimensions of NTU-CBT are smaller than those of MNI 305 template in all directions, especially in height and length. The length, width, height, and volume of NTU-CBT are 88.9%, 97.9%, 84.3%, and 73.6% of that of MNI template, respectively. NTU-CBT is not only smaller than MNI template in size but also different in dimensional ratios. Among the 3 dimensional ratios, the Width/Length ratio of the Chinese brain template is greater than that of MNI template. The overlay of both templates is shown in Figure 1.

Table 1. The hemispheric features between Chinese males and females. LAB, length of anterior brain; LPB, length of posterior brain; HSB, height of superior brain; HIB, height of inferior brain; WLB, width of left brain; WRB, width of right brain. (in mm. * P<0.0001)

Hemispheric feature	95 subjects Mean (SD)	Male (50) Mean (SD)	Female (45) Mean(SD)	T-test
AC-PC	25.3 (1.57)	25.6 (2.97)	24.9 (5.1)	0.66
LAB	69.8 (4.67)	65.7 (2.97)	64.1 (3.09)	2.55
LPB	70.8 (3.57)	70.5 (4.49)	69.0 (4.73)	1.64
HSB	42.3 (2.8)	71.9 (3.40)	69.5 (3.27)	3.55*
HIB	69.5 (3.03)	42.9 (3.09)	41.7 (2.43)	2.10
WRB	69.5 (3.03)	70.8 (2.89)	68.1 (2.50)	4.94*
WLB	69.6 (2.99)	70.8 (2.76)	68.4 (2.44)	4.50*

Table 2. Cerebral dimensions between NTU-CBT and MNI template. L, length; W, width; H, Height. (* P<0.0001) [8]

	NTU-CBT (n=95)	MNI (n=305)	Difference	CBT/MNI ratio
Length	16.0±0.74 cm	18.0±0.2 cm	-2.00* cm	88.9%
Width	13.9±0.57 cm	14.2±0.2 cm	-0.26 cm	97.9%
Height	11.3±0.54 cm	13.4±0.2 cm	-2.10* cm	84.3%
W/L ratio	87.1%	78.9%	+8.2%	
H/W ratio	81.1%	94.4%	-13.3%	
H/L ratio	70.6%	74.4%	-3.8%	

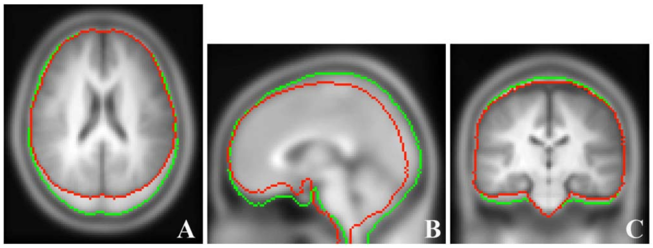

Fig. 1. Overlay brain contour of the two templates. Red line represents NTU-CBT contour and green line indicates MNI template contour. (A) Axial view. (B) Sagittal view. (C) Coronal view.

Due to lack of exact original hemispheric features of MNI template, we manually measured the hemisphere features of MNI template (AC-PC, LAB, LPB, LSB, LIB, WRB and WLB) by MIPAV. The comparisons of these hemispheric features between NTU-CBT and MNI template are shown in Table 3. The most significant differences are LPB and HSB. Both features in NTU-CBT are smaller than those in MNI template by more than 20%, whereas the others in NTU-CBT are smaller by around 3~6%. The LPB and HSB contribute mostly to the dissimilarity of MNI and NTU-CBT.

Table 3. Comparison of hemisphere feature between NTU-CBT and MNI template.

Hemispheric feature	NTU-CBT (mm)	MNI (mm)	Difference (mm)	Difference ratio
AC-PC	25.3	26.5	-1.2	-4.7%
LAB	65.0	69.0	-4.0	-6.2%
LPB	69.8	84.5	-14.7	-21.1%
HSB	70.8	90.0	-19.2	-27.1%
HIB	42.3	44.0	-1.7	-4.0%
WRB	69.5	73.0	-3.5	-5.0%
WLB	69.6	72.0	-2.4	-3.4%

The results of foot tapping fMRI study are show in Figure 2 with threshold T value at 4 and cluster size 100. The activation areas were both located in upper medial frontal lobe, but the activation region on NTU-CBT was deeper into the interhemispheric fissure than that on MNI template. The result applying to NTU-CBT was more compatible with the traditional motor homunculus illustration [10].

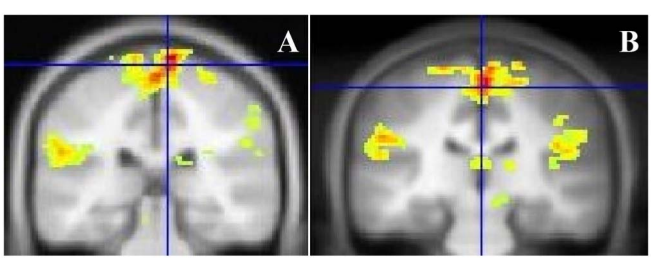

Fig. 2. Coronal view of main activation areas of foot tapping task. Both were located in upper medial frontal lobe, but the result on NTU-CBT was deeper into the interhemispheric fissure, which was more compatible with the traditional motor homunculus illustration. (A) MNI template. (B) NTU-CBT.

The axial slices of activation voxels are further displayed in Figure 3. The distribution of activation areas on both templates was similar, however, we can see clearly at the last row of MNI template in Figure 3, the activated voxels inside the white dotted rectangular area were apparently out of cortical margin, which was unreasonable anatomically and physiologically. All activated voxels on motor cortex shown in NTU-CBT were inside the cortical margin.

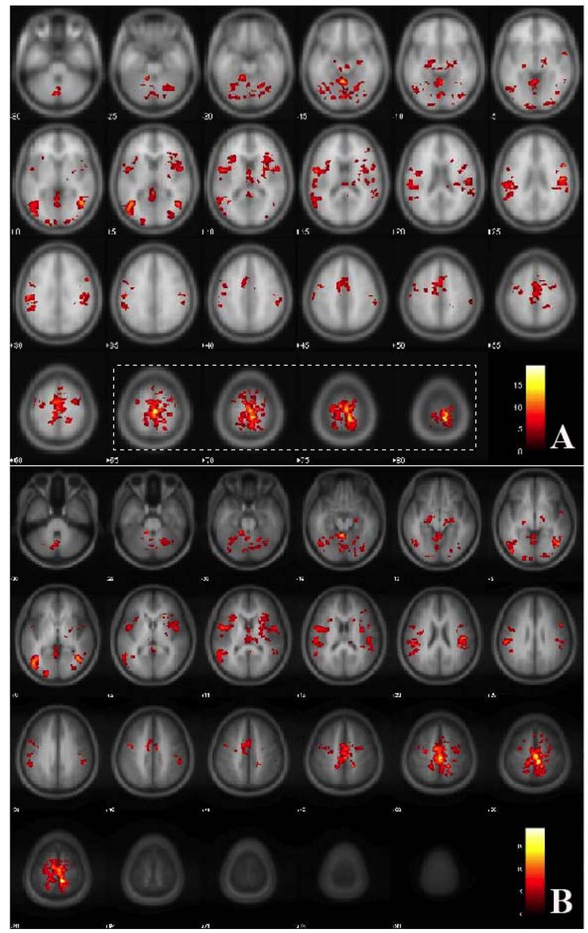

Fig. 3. Slice display of activation voxels of foot tapping task. There was obvious discrepancy of the distribution of activation voxels, with more compact activation regions and less activation voxels when using NTU-CBT. (A) MNI template. (B) NTU-CBT.

The distribution of activated voxels in visual stimulation experiment was displayed in Figure 4. The threshold T value was set at 4 and cluster size was 100. The results also revealed a mismatch between applying to MNI template and NTU-CBT, with more conservative activation areas on the later one.

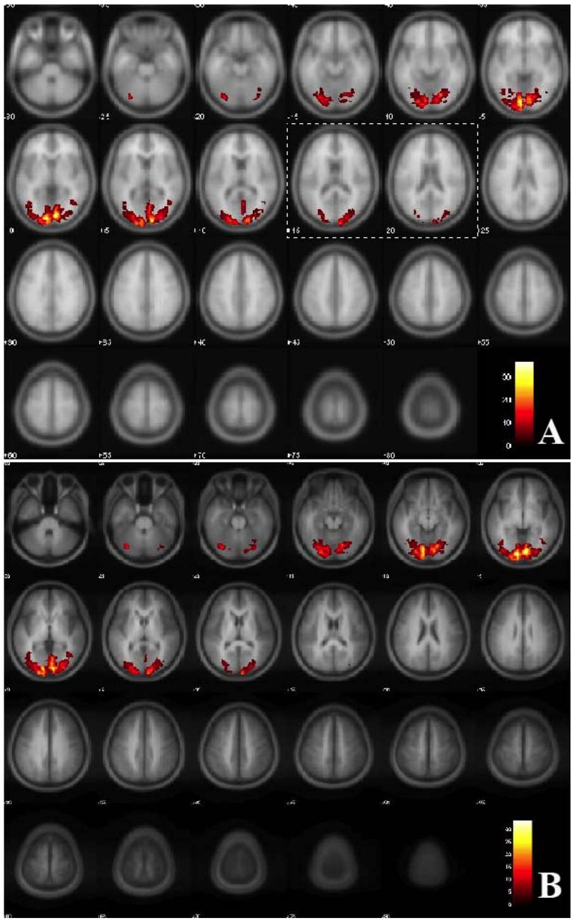

Fig. 4. Slice display of activation voxels of checkerboard visual stimulation. The activation areas on NTU-CBT are relatively conservative with less activation voxels and slices. (A) MNI template. (B) NTU-CBT.

We further calculated the number and volume of activation voxels in these fMRI experiments. Each number and volume in NTU-CBT was smaller than that of the MNI template (Table 4).

Table 4. Comparison of the average number and volume of activation voxels between NTU-CBT and MNI template in different fMRI tasks.

Stimulation	Voxel Number		Voxel Volume		CBT/MNI Ratio
	CBT	MNI	CBT	MNI	
Visual	5666	7020	45328	56160	80.7%
Left ankle	12722	17474	101776	139792	72.8%

IV. DISCUSSION AND CONCLUSION

This novel morphologic analysis suggested significant differences in size and shape between NTU-CBT and MNI template. The size of NTU-CBT is smaller than that of MNI template, especially in height and length. As for brain shape, NTU-CBT is wider, flatter, and more circular rather than elliptical shape of MNI template.

However, the male-to-female ratio in NTU-CBT is 1.1 compared to 3.62 in MNI template. This overt male-to-female ratio in MNI template may probably contribute to a bigger average brain template, and this ratio discrepancy may also be responsible somehow for the morphologic difference between NTU-CBT and MNI template.

In our pilot fMRI study, the distributions of major activation areas were similar on both templates. Nonetheless, there were still certain noticeable differences between using NTU-CBT and MNI template, with more reasonable anatomical interpretation in foot tapping task and visual stimulation task. These discrepancies may result from several factors. The main reason is probably the disproportionally larger size of MNI template, which may lead to misleading interpolation. When the original fMRI dataset of an ordinary Chinese subject was interpolated to the MNI template, the main activation region would probably be stretched or distorted and later distributed to more slices. This process could explain the reason why there were more compact activation regions and less activation voxels when using NTU-CBT.

Furthermore, if an original activation area possessed voxel number just a little bit below the threshold of cluster size, this area could probably turn out to be visible on MNI template due to the amplifying effect of interpolation to MNI template. This could account for the more conservative results when using NTU-CBT.

Even if there are significant morphologic differences between NTU-CBT and MNI template, more evidences are required to determine whether MNI template should be replaced by NTU-CBT in neurocognitive studies for Chinese subjects, and this could be answered by further functional brain labeling.

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