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MAJOR PAPER

Effects of Image Distortion Correction on Voxel-based Morphometry

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Purpose: We aimed to show that correcting image distortion significantly affects brain volumetry using voxel-based morphometry (VBM) and to assess whether the processing of distortion correction reduces system dependency.

Materials and Methods: We obtained contiguous sagittal T_1-weighted images of the brain from 22 healthy participants using 1.5- and 3-tesla magnetic resonance (MR) scanners, preprocessed images using Statistical Parametric Mapping 5, and tested the relation between distortion correction and brain volume using VBM.

Results: Local brain volume significantly increased or decreased on corrected images compared with uncorrected images. In addition, the method used to correct image distortion for gradient nonlinearity produced fewer volumetric errors from MR system variation.

Conclusion: This is the first VBM study to show more precise volumetry using VBM with corrected images. These results indicate that multi-scanner or multi-site imaging trials require correction for distortion induced by gradient nonlinearity.

Keywords: ***brain volumetry, distortion correction, gradient field nonlinearities, magnetic resonance imaging, voxel-based morphometry***

Introduction

Voxel-based morphometry (VBM)[1] using 3-dimensional T_1-weighted (3D-T_1) magnetic resonance (MR) images has been employed to estimate local brain volume.[2–5] Previous studies investigated whether distortion might cause error in estimating brain volume and evaluated the accuracy of various methods for correcting distortion.[6–8] However, those reports did not investigate the effect of distortion correction with regard to computational brain volumetry analyses (i.e., boundary shift integral,[9] VBM,[1] tensor-based morphometry,[10] and atlas-based volumetry[11]). We agree that use of images corrected for distortion improves analysis but believe additional study is required of VBM that includes spatial normalization. This study has 2 aims. The first is to show that correcting distortion significantly affects brain volumetry using VBM. Because analytical procedures that include normalization may reduce the influence of distortion correction in VBM and obscure the effects of correction, it is important to confirm the need for correction in

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VBM. Following distortion correction, regions of increased volume would correspond to regions of reduced volume caused by distortion, and regions of reduced volume would correspond to those with increased volume caused by distortion.

Our second aim is to assess whether system dependency decreases in the processing of distortion correction. In multi-site studies, data obtained using different MR imaging systems are mixed in the same analytical flow. Consequently, previous reports of multi-site studies[12–14] showed less precise brain volumetry as a result of heterogeneous signal intensity and low signal-to-noise ratio (SNR). The degree of image distortion depends on such variables within the MR imaging system.[15] However, no reports have shown reduced volumetric precision of VBM as a result of using distorted images.

Materials and Methods

Subjects

Twenty-two healthy volunteers (17 men, 5 women; aged 23 to 47 years, mean age 31.1 ± 7.3 years) underwent MR imaging at 1.5 and 3 tesla, with 3D-T_1 images obtained the same day. A board-certified radiologist (O.A.) inspected the images and found none of the following in any subject: brain tumor, infarction, hemorrhage, brain atrophy, cognitive impairment, or white matter lesions graded higher than grade 2 of Fazekas classification.[16] Cognitive impairment was screened with a mini-mental state examination, and T_2-weighted images were used to evaluate white matter lesions. The ethical committee of our institution approved the study, and written informed consent was obtained from all participants.

MR imaging protocol

We obtained MR imaging data using 2 systems. The first was a 1.5T scanner (Signa EXCITE HD, GE Healthcare, Waukesha, WI, USA; 33 mT/m maximum strength, 120 T/m/s slew rate) with a quadrature head coil used for transmission and reception. We used 3D magnetization-prepared rapid gradient-echo (3D-MPRAGE) to obtain 184 contiguous sagittal T_1-weighted images with slice thickness, 1.3 mm; repetition time (TR)/echo time (TE), 3000 ms/3.9 ms; inversion time (TI), 1000 ms; flip angle, 8°; field of view (FOV), 24 cm; number of excitations (NEX), one; and matrix, 192×192 pixels. We used 2D fast spin-echo (2D-FSE) to obtain 48 axial T_2-weighted images with slice thickness, 3 mm; TR/TE, 3000 ms/100 ms; echo train length, 16; FOV, 24 cm; NEX, one; and matrix, 256×256 pixels.

The second system was a 3T scanner (Signa EXCITE HDx, GE Healthcare; 40 mT/m maximum strength, 150 T/m/s slew rate) with a quadrature head coil used for transmission and reception. We used 3D-MPRAGE to obtain 170 contiguous sagittal T_1-weighted images with slice thickness, 1.3 mm; TR/TE, 2300 ms/2.8 ms; TI, 900 ms; flip angle, 8°; FOV, 26 cm; NEX, one; and matrix 256×256 pixels. We used 2D-FSE to obtain 48 axial T_2-weighted images with slice thickness, 3 mm; TR/TE, 3000 ms/97 ms; echo train length, 16; FOV, 24 cm: NEX, one; and matrix, 256×256 pixels. We employed scanning protocols using the protocol of the Alzheimer's Disease Neuroimaging Initiative.

Image preprocessing for VBM

We used Statistical Parametric Mapping 5 (SPM5)[17] software for volumetric analysis, nonparametric nonuniform intensity normalization (N3) software[18] for intensity bias correction, and spherical harmonics description of gradients (SHDG)[8] for gradient nonlinearity distortion correction. Image distortion in MR has 6 potential sources–scale errors (linear) in gradient fields, shimming anomalies of the main magnet, chemical shift, B_o eddy currents, nonlinearities of gradient fields, and magnetic susceptibility variations in various anatomical structures.[19] We can correct nonlinearities of gradient fields and know their influence is large, but we cannot correct magnetic susceptibility variations in anatomical structures. Therefore, we focused only on image distortion caused by nonlinearities of gradient fields.

The various distortion correction methods include SHDG, phase mapping,[20] adoption of a specially constructed phantom,[21] and the use of 2 frequency-encoding gradients.[22] We employed SHDG correction for nonlinearities of the gradient fields using the same method described by Jovicich and colleagues,[8] which employs information based on the design of the gradient coils; we used MR-specific information, such as the gradient correction coefficients. SHDG correction can correct image distortion caused by nonlinearities of the gradient fields but not distortion caused by other factors, such as magnetic susceptibility variations in various anatomical structures. Jovicich's group[8] reported the efficiency of SHDG correction in a study that showed distorted areas using a grid phantom and differences in brain surface boundaries using images of the human brain. Therefore, we further evaluated this method for VBM that included normalization.

We processed 3D-MPRAGE images with and without SHDG correction in SPM5 after N3 processing. In SPM5, 3D-MPRAGE images in native space were bias-corrected, spatially normalized, and segmented into images (i.e., gray matter, white matter, and cerebrospinal fluid); voxel size of the spatially normalized images was $2 \times 2 \times 2$ mm. We changed the affine regularization space template in the International Consortium for Brain Mapping from the European to the East Asian brain template. In the modulation step, we multiplied the voxel values of the spatially normalized gray and white matter images by a measure of the relative volumes of the warped and unwarped structures that were derived from the nonlinear step of spatial normalization (Jacobian determinant).

For each subject, we added the spatially normalized image of gray matter and that of white matter and defined this as the brain image in this study. Spatially normalized brain images were smoothed with 8-mm isotropic Gaussian kernels. Four sets of each processed volume were obtained as follows: (A) brain images with SHDG correction obtained with the 1.5T system; (B) brain images without SHDG correction obtained with the 1.5T system; (C) brain images with SHDG correction obtained with the 3T system; and (D) brain images without SHDG correction obtained with the 3T system.

To test for a statistically significant effect of distortion correction, we prepared differential images (DI). DI-1.5 was defined as (brain image with SHDG correction obtained with the 1.5T system) − (brain image without SHDG correction obtained with the 1.5T system). In statistical analysis of DI-1.5 for the 22 subjects, we assessed the effect of SHDG correction.

To investigate reduction in system dependency, we prepared DI-C and DI-nonC: DI-C was defined as (brain image with SHDG correction obtained with the 1.5T system) − (brain image with SHDG correction obtained with the 3T system), and DI-nonC was defined as (brain image without SHDG correction obtained with the 1.5T system) − (brain image without SHDG correction obtained with the 3T system). In statistical analysis of DI-Cs and DI-nonCs of the 22 subjects, we assessed whether SHDG correction resulted in fewer volumetric errors caused by variation in MR system.

Statistical analyses for the effect of distortion correction

We compared estimated brain volumes with and without SHDG correction using the DI-1.5s of the 22 subjects and analyzed the DI-1.5s with SPM5, employing the framework of the general linear model. To test hypotheses with respect to regionally specific group effects, we tested the estimates with one-sample t-test using VBM. In this analysis, ''plus regions'' were regions increased by SHDG correction, and ''minus regions'' were regions reduced by SHDG correction. The significance of each region was estimated by distributional approximations from the random Gaussian fields theory. $P < 0.05$, corrected with family-wise error (FWE) in voxel difference and cluster size greater than 30 voxels, was considered statistically significant.

Statistical analyses for reduction of system dependency

We examined whether SHDG correction could reduce brain volumetric errors caused by MR system variation. We analyzed the DI-Cs and DI-nonCs of the 22 subjects using SPM5, employing the framework of the general linear model. To test hypotheses with respect to regionally specific group effects, we compared estimates with 2 linear contrasts using VBM. Correction of image distortion by SHDG indicated significant difference between DI-C and DI-nonC. The significance of each region was estimated by distributional approximations from the theory of random Gaussian fields. $P < 0.05$, corrected with FWE in voxel difference and cluster size greater than 30 voxels, was considered statistically significant.

We prepared 2 design matrices to estimate system dependence in regions increased or reduced by nonlinearities of gradient fields. We used the first matrix (Fig. 3) to investigate system dependence inside regions reduced by SHDG correction. In analysis using this matrix, we estimated significant minus regions in the DI-nonC of the 22 subjects by VBM (uncorrected $P < 0.05$) and set these minus regions as an inclusive mask. These significant minus regions indicated that volume expansion caused by nonlinearities of gradient fields was greater in the 3T system than the 1.5T system.

We used the second matrix (Fig. 4) to investigate system dependence within regions increased by SHDG correction. In analysis using this matrix, we estimated significant plus regions in the DI-nonC of the 22 subjects by VBM (uncorrected $P < 0.05$) and set these plus regions as an inclusive mask. These significant plus regions indicate that volume reduction caused by nonlinearities of gradient fields was greater in the 3T system than the 1.5T system.

Results

Results of comparison between images with and without SHDG correction

Various regions of the brain showed significantly reduced (Fig. 1) and increased (Fig. 2) volumes fol-

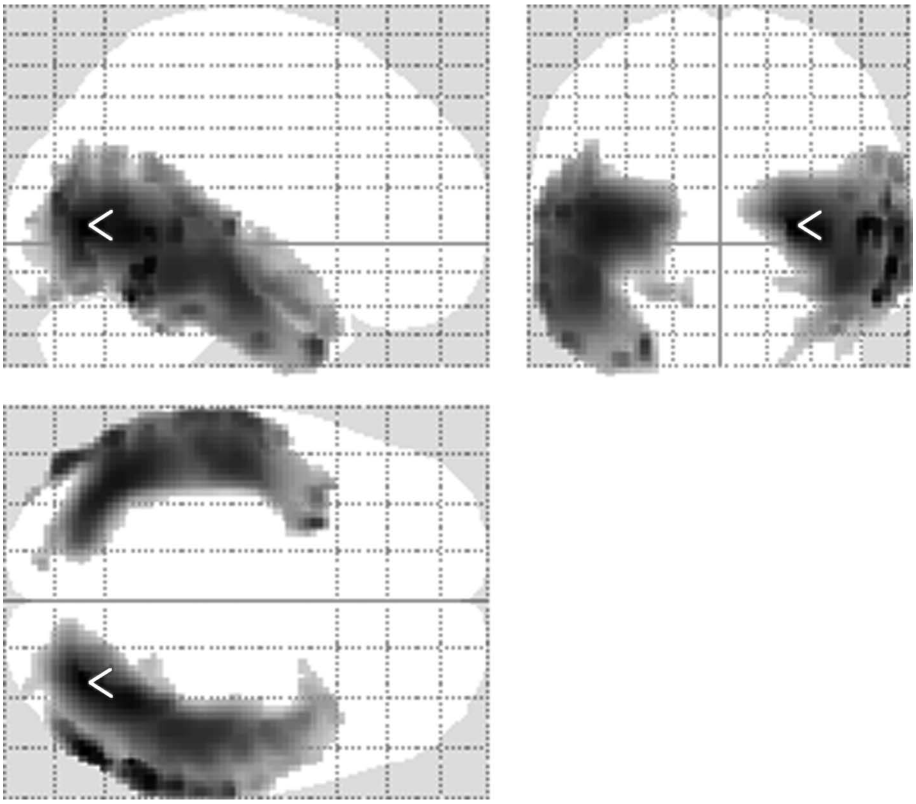

Fig. 1. The figure is a ''glass brain'' that indicates all regions in which brain volume was significantly reduced on corrected images compared to those without correction (gray scale, voxel with maximum effect indicated by red pointer). $P < 0.05$, corrected with family-wise error (FWE) in voxel difference and cluster size greater than 30 voxels, was considered statistically significant.

lowing SHDG correction. Figure 1 shows all regions in which corrected images demonstrated significantly reduced local brain volume compared with uncorrected images. The Montreal Neurological Institute (MNI) coordinates of local maxima were 28, -70, 6 ($P < 0.001$, T value = 14.97, cluster size = 12597). Figure 2 shows all regions in which corrected images demonstrated significantly increased local brain volume compared uncorrected images. MNI coordinates of local maxima were 22, 4, 54 ($P < 0.001$, T value = 21.61, cluster size = 24441).

Results of brain volumetry error caused by MR system variation

SHDG correction decreased the system dependence of estimated brain volumes. Figure 3 shows all regions in which DI-nonC using uncorrected images had significant minus regions in comparison with DI-C using corrected images. In other words, brain volumetry was more system dependent using uncorrected images than corrected images; SHDG correction decreased system dependence within regions reduced by correction. MNI coordinates of local maxima were -46, -28, -12 ($P < 0.001$, T value = 12.38, cluster size = 5573). Figure 4 shows all regions in which the DI-nonC of uncorrected images demonstrated significant plus regions in comparison with the DI-C of corrected images. In other words, brain volumetry was more system dependent using uncorrected images than corrected images; SHDG correction reduced system dependence within regions increased by correction. MNI coordinates of local maxima were -18, -8, 50 ($P < 0.001$, T value = 10.07, cluster size = 7727). Figure 5 shows T_1WI with and without SHDG correction for a single subject.

Discussion

In our VBM study, we detected areas whose volumes increased or reduced by image distortion caused by nonlinearities of the gradient fields. Volume was reduced in the area around the temporal lobe and increased in the area around the frontal and parietal lobes. Thus, the influence of image distortion extends to the deep regions of the brain as well as surface regions. The results of com-

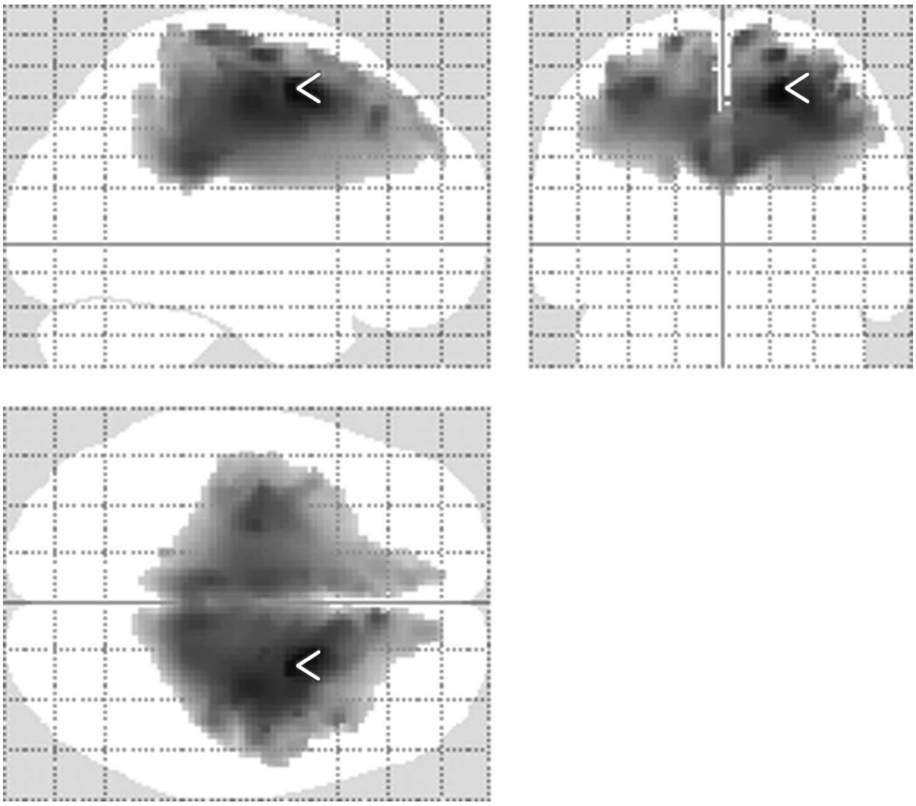

Fig. 2. The figure is a ''glass brain'' that indicates all regions in which brain volume was significantly increased on corrected images compared to those without correction (gray scale, voxel with maximum effect indicated by red pointer). $P<0.05$, corrected with family-wise error (FWE) in voxel difference and cluster size greater than 30 voxels, was considered statistically significant.

parison between corrected and uncorrected images (Figs. 1, 2) seem to deviate from the orthogonal frame of the gradients because the axis of the figures deviates from that frame; the images were obtained with most subjects lifting their chins against that frame. Therefore, we think that the areas of significant difference in our results are distributed according to the orthogonal frame of the gradients. The present study is the first to clarify the effect of SHDG correction on VBM.

McRobbie and associates showed that the amount of image distortion differs for each system.[15] Because distortion influences the results of VBM analysis, we considered the distortion to be related to system dependence. Therefore, we assessed whether image distortion correction processing resulted in reduced system dependency. The results (Figs. 3, 4) showed that SHDG correction reduced system dependency. Unfortunately, this result does not prove that distortion correction completely eliminates system dependency, but it does provide insight into the need for correcting image distortion in multi-site studies. Even in a study using a single system, image distortion affects analytical results because spatial placement of the main magnetic field center and the brain center influences the deformation volume due to distortion. This spatial placement in imaging differs among subjects.[8] In addition, the use of image distortion correction is strongly recommended in multi-site studies to minimize volumetric errors caused by system variation. In many institutions, however, VBM researchers may not always have access to MR-specific information or vendor-specific technical information, such as the gradient correction coefficients that should be used to perform SHDG correction. Therefore, previous studies may have utilized VBM studies using uncorrected images.

The major limitation of our study is that we cannot know the true brain volume. Neither can we explain whether the SHDG method performed excessive correction in this study. Therefore, we could demonstrate only that in brain volumetry using VBM, volume differed between SHDG-corrected and noncorrected images, and volumetry error due to system variation was decreased when image distortion correction was employed. Unfortunately, we could not show that VBM analysis with distor-

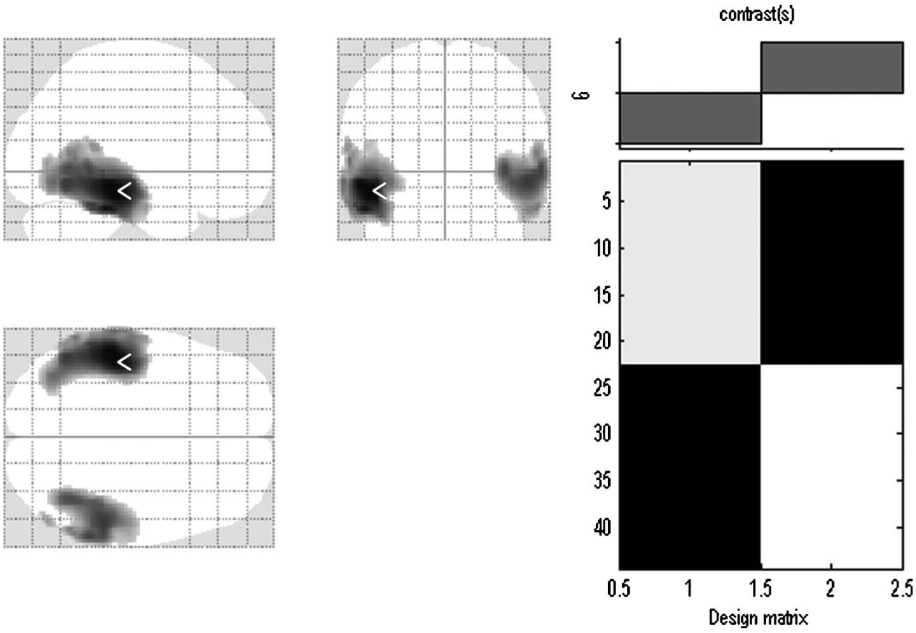

Fig. 3. Left side, a ''glass brain'' that indicates all regions in which system dependence was significantly less in corrected images than uncorrected images (gray scale, voxel with maximum effect indicated by red pointer). This figure showed system dependence inside increased regions caused by image distortion. Right side, design matrix. The left group in the design matrix comprised differential images (DI)-nonC and the right group, DI-C. P value < 0.05, uncorrected in voxel difference and cluster size greater than 30 voxels, was considered statistically significant.

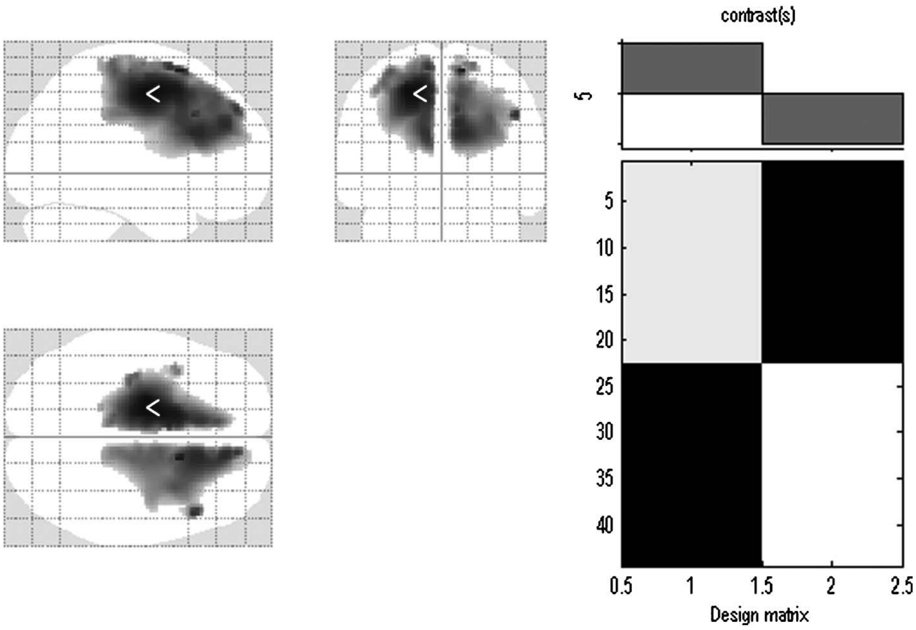

Fig. 4. Left side, a ''glass brain'' that indicates all regions in which system dependence was significantly less in corrected images than uncorrected images (gray scale, voxel with maximum effect indicated by red pointer). This figure showed system dependence inside reduced regions caused by image distortion. Right side, design matrix. The left group in the design matrix comprised differential images without correction (DI-nonC) and the right group, those with correction (DI-C). $P < 0.05$, uncorrected in voxel difference and cluster size greater than 30 voxels, was considered statistically significant.

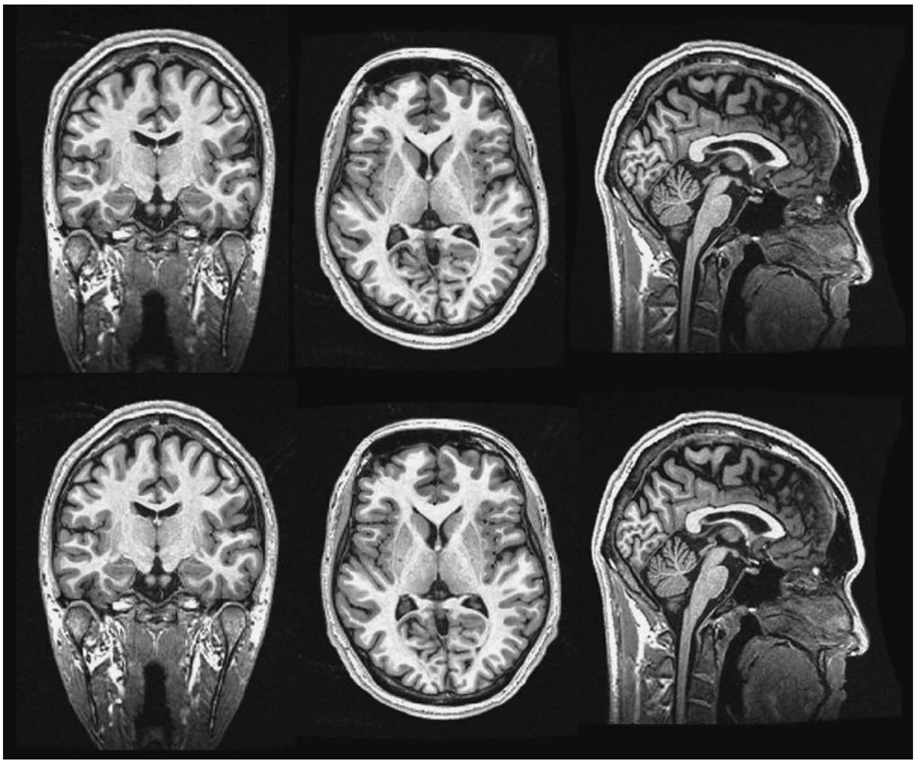

Fig. 5. Upper side, T_1W-weighted imaging (T_1WI) with spherical harmonics description of gradients (SHDG) correction; lower side, T_1WI without SHDG correction of a subject in the present study. Figure shows representative coronal, axial, and saggital slices of the original structural T_1 volume.

tion correction more accurately estimated brain volume. However, in their phantom study, Jovicich's group showed that the phantom volume from a corrected image was much closer to the true phantom volume.[8] We performed a similar inspection and obtained a similar result. Therefore, we can conclude that VBM analysis using a corrected image provides a result near to the true brain volume.

Conclusions

We believe this is the first VBM study to show that the use of corrected images can reduce volumetric errors caused by system variations. These results indicate that correction of distortion induced by gradient nonlinearity is mandatory in multi-scanner or multi-site imaging trials.

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