Structural Brain Asymmetry as Revealed by 3D Texture Analysis of Anatomical MR Images

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Abstract

We used 3D texture analysis approach to examine the structural brain asymmetry. The method is based on extended, multi-sort co-occurrence matrices that employ intensity, gradient and anisotropy image features in a uniform way. The asymmetry in normals and in patients with pathological findings was evaluated on a large sample of 310 MRI-T1 images with the focus on the asymmetry differences associated with gender. The analysis revealed higher asymmetry in males comparing females (t=7.23, $p < 10^{-6}$ in young and t=2.65, $p = 0.012$ in elderly subjects). Separate analysis of white and gray matters showed significant asymmetry increase with age (F=21.43, $p < 10^{-6}$) of gray but not white matter.

Keywords: *brain asymmetry, 3D texture, co-occurrence*

1 Introduction

Different aspects of anatomical asymmetry of the human brain were studied in a number of works. Depending on a specific goal, various definitions of the "asymmetry" term itself and a range of methods were suggested to estimate the asymmetry degree. On the level of its gross shape, the brain may be considered as "almost symmetric" against the mid-sagittal plane and the image processing problem is often posed as an automatic detection of mid-sagittal plane in 3D brain images (e.g., [6], [2]). Besides, even on the low-resolution level of brain shape consideration there were relatively well separated clusters found associated with gender and certain ethnic groups [12]. The gross volumetric asymmetries in norm (hemispheres in total, brain compartments, and different intracranial structures) and their relations with age and gender were studied in several works (see, for example, results of in-vivo measurements of 200 normal brains documented in [3]). Other neurological studies concentrated on such particular anatomical brain asymmetries as asymmetry of major sulci in their extent, curvature, and surface complexity with respect to age and changes caused by Alzheimer's disease [11], an asymmetry in the depth of central sulcus and its relationships with handedness and gender [1], volumetric asymmetry of planum temporale in boys and girls [8]. Research works done in image processing domain mostly attend to develop methodological base of asymmetry analysis. For instance, Thirion et al. [10] capitalize upon 3D vector field operators to detect the mid-plane, compute and fuse dissymmetry information over a population, and determine significantly dissymmetrical regions. Another method of the analysis and visualization of cerebral brain asymmetry is reported in [7]. Along with more specific anatomical studies, they demonstrated that high intra- and inter-subject variability of brain regions leaving almost no chance for straightforward approaches based on "mirrored-point" analyses. In this paper, we study structural brain asymmetry by means of 3D texture analysis method suggested in [4]. The method is based on extended, multi-sort co-occurrence matrices that employ intensity, gradient and anisotropy image features in a uniform way. The asymmetry is regarded as a dissimilarity of 3D gray-scale image patterns, as detected by anatomical MRI-T1 in the left and right brain hemispheres. The purpose of the analysis was to investigate structural brain asymmetry in normal volunteers and in patients with pathological findings with the particular attention to asymmetry differences associated with gender. The analysis is based on a large sample of 310 high-resolution MRI-T1 brain images of well-matched groups of subjects. In our best knowledge, this is the first work on structural brain asymmetry evaluation by 3D texture analysis.

2 Materials and methods

Subjects. Our central study of asymmetry differences associated with gender was performed on age- and gender-

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matched group GR-GEND1 of 210 young healthy subjects consisting of 103 males and 107 females (mean age 24.8, STD 3.97 years). For an additional analysis of gender-related asymmetry in elderly subjects the group GR-GEND2 of 33 healthy individuals (14 males and 19 females, mean age 78.4 years) was collected. Changes of brain asymmetry associated with normal aging were evaluated on the group GR-AGING of 55 subjects that was conditionally sub-divided into the young subgroup (33 subjects aged 16-25 years, 17 males and 16 females, sub-sample of GR-GEND1) and "aged" subgroup (22 subjects, 50-70 years, 11 males and 11 females). Asymmetry changes caused by the brain pathologies were evaluated on the group GR-PATH of 40 subjects including 19 patients (11 males and 8 females) with brain lesions (cerebral infarctions, severe head trauma, and intra-cerebral hemorrhage) and 21 controls (11 males and 10 females).

MR image data. MR acquisition of all groups except GR-GEND2 was performed on a Bruker 3T Medspec 100 system equipped with a bird cage quadrature coil using a T1-weighted 3D MDEFT protocol: FOV 220x220x192 mm, matrix 256x256, 128 sagittal slices, voxel size 0.9 x 0.9 mm, 1.5 mm slice thickness, scanning time 15 min. Original image data of group GR-GEND2 were acquired on a 1.5T Siemens scanner (MPRAGE sequence, TR 11.4 ms, TE 4.4 ms, 128 slices, matrix 256x256, voxel size 0.9x0.9x1.5 mm). All scan data were segmented [5], interpolated to an isotropical voxel size of 1.0 mm by a fourth-order b-spline method [9], and aligned with the stereotactical co-ordinate system where the mid-sagittal plane lying in the pre-defined vertical plane passing through the image origin [5]. Finally, brain datasets were cropped into a minimum box of 160x200x160 mm extent (Fig. 1).

The method. We employed the extended multi-sort co-occurrence matrices [4] as detailed descriptors of spatial 3D image structure. For a semi-formal definition of these matrices, let us consider an arbitrary voxel pair (i,k) defined on a discrete 3D voxel lattice by voxel indices $i = (x_i, y_i, z_i)$ and $k = (x_k, y_k, z_k)$ and with the Euclidean distance $d(i,k)$. Let us denote their intensities by $I(i)$ and $I(k)$, local gradient magnitudes by $G(i)$, $G(k)$ and the angle between gradient vectors by $a(i,k)$. Then the general, six-dimensional co-occurrence matrix can be defined as:

$$W = ||w(I(i), I(k), G(i), G(k), a(i,k), d(i,k))||,$$
$$a(i,k) = \cos^{-1}\left(g(i) \bullet g(k)\right),$$

where $g(i) \bullet g(k)$ is the dot vector product and $g(i)$, $g(k)$ are normalized intensity gradient vectors at voxel positions i and k. Gradient vector components can be derived by any suitable 3D operator. Since we are dealing with high frequency textures, we used a filter with the small 3x3x3 window [13]. Due to the page limit, a formal definition of matrices, evaluation of their properties, results of a sensitivity study, and matrix normalization procedure are given in [4]. Note only that in this study matrix bining parameters were 8 intensity bins (32 units each), 6 gradient magnitude bins (160 gradient units each), 6 angle bins (30 degrees each) and 4 distance bins (d=1-4 mm).

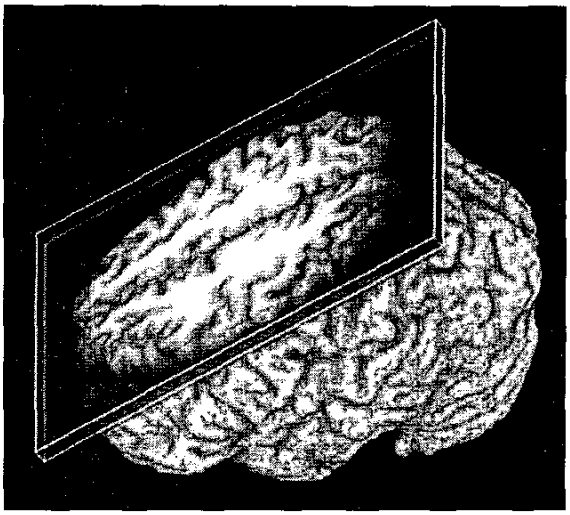

Figure 1. An example of segmented high-resolution MR-T1 images used in this study.

Asymmetry measurements were performed by calculating $L1$ distance (normalized sum of absolute element-by-element differences) between the co-occurrence descriptors of 3D image patterns in the left and right brain hemispheres. The correctness of such comparison of typically "reflected" image patterns in brain hemispheres is enabled by the matrix reflection/rotation invariance [4]. When calculating $L1$ distance, matrices computed for the left and right hemispheres are treated as two feature vectors with cell-by-cell correspondence of elements. No feature selection is used. Thus, in all the cases the "asymmetry value" term corresponds to the $L1$ distance between co-occurrence descriptors of brain hemisphere images.

3 Results

Asymmetry in normal volunteers vs. neurological patients. We start with the comparison of brain asymmetry in healthy subjects and patients with brain lesions using group GR-PATH. Presence of lesions obviously changes the degree of "normal" inter-hemispheric asymmetry what should be detectable by the method. Comparative analysis of asymmetry variation between subgroups of healthy subjects and patients (Fig. 2) was performed using double-sided t-

test with unequal variance. It was found that pathological brains are significantly more asymmetric (mean asymmetry value 0.152 against 0.081, t=5.01, $p < 10^{-5}$). As it was expected, the variation of asymmetry degree in patients is much wider (STD 0.06 vs. 0.02) and depends on the lesion extent. In addition, asymmetry of 22 male and 18 female subjects of group GR-PATH was evaluated by the univariate analysis of variance (ANOVA) method using health status (norm/pathology) and gender as two independent factors. Surprisingly, even under condition of great inter-subject diversity, the ANOVA reported significant gender-related asymmetry difference (males being more asymmetric, F=5.72, $p = 0.022$).

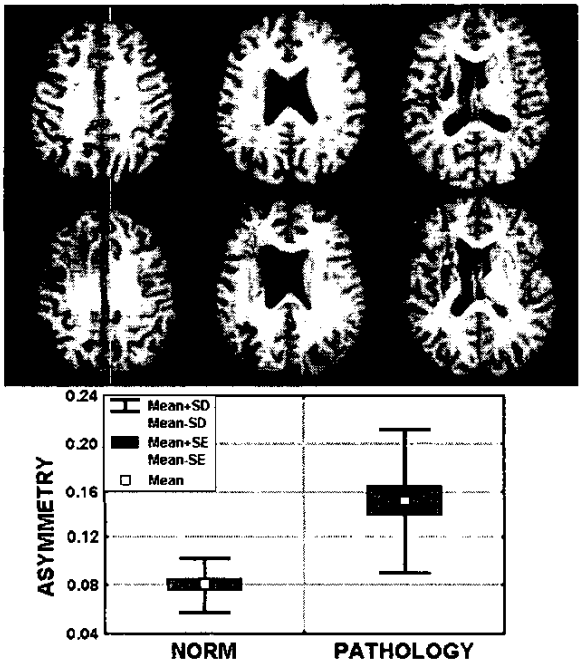

Figure 2. Brain asymmetry in normal volunteers vs. neurological patients. Example of two patients with moderate (top 3 slices) and severe (middle 3 slices) cerebral infarctions and statistical results of asymmetry comparison (bottom, N=40).

Gender-related asymmetry differences in healthy young subjects. This analysis was done using 210 subjects of group GR-GEND1 (Fig. 3). Comparison of the asymmetry degree revealed significantly higher asymmetry in males than in females (mean value 0.145 against 0.101, t=7.23, $p < 10^{-6}$).

Gender-related asymmetry differences in healthy elderly subjects. It is commonly known that normal aging leads to various changes in brain structure such as general atrophy, ventricle enlargements, diffuse white matter hypointensity, and enlarged periventricular spaces (see 6 subjects depicted in Fig. 4 as an example). Thus, we were interested in the degree of asymmetry in healthy elderly subjects as represented by group GR-GEND2. In spite of these strong individual distinctions caused by age, male brains were found to be more asymmetric again (mean asymmetry 0.110 against 0.069 in females). As predicted, the significance of gender-related differences in asymmetry in elderly subjects is lower (t=2.65, $p = 0.012$) than in group GR-GEND1. Note that a comparison of absolute asymmetry values for groups GR-GEND1 and GR-GEND2 is not viable because of different MRI scanners.

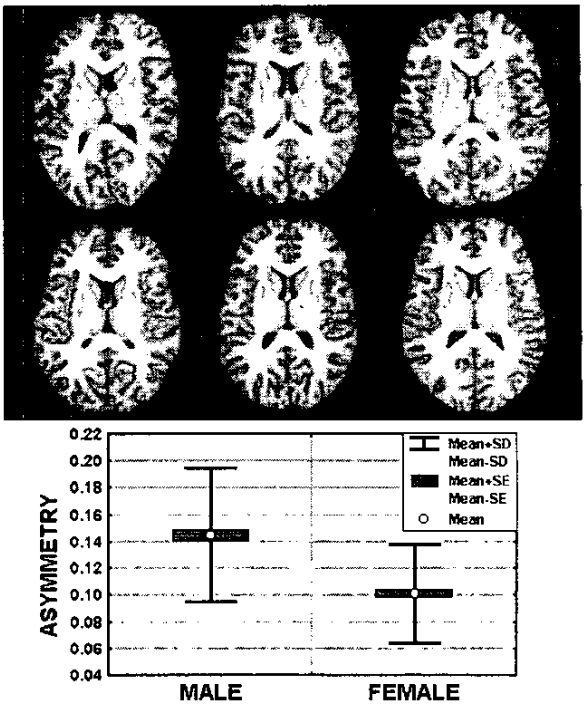

Figure 3. Gender-related asymmetry differences in healthy young subjects. Example slices of 3 male (top) and 3 female (middle) subjects and asymmetry evaluation results (bottom, N=210).

Changes of asymmetry with normal aging. This particular topic was accounted using group GR-AGING consisting of two gender-matched subgroups of young and aged subjects. In order to eliminate gender-related asymmetry variability, the analysis was performed by ANOVA with age

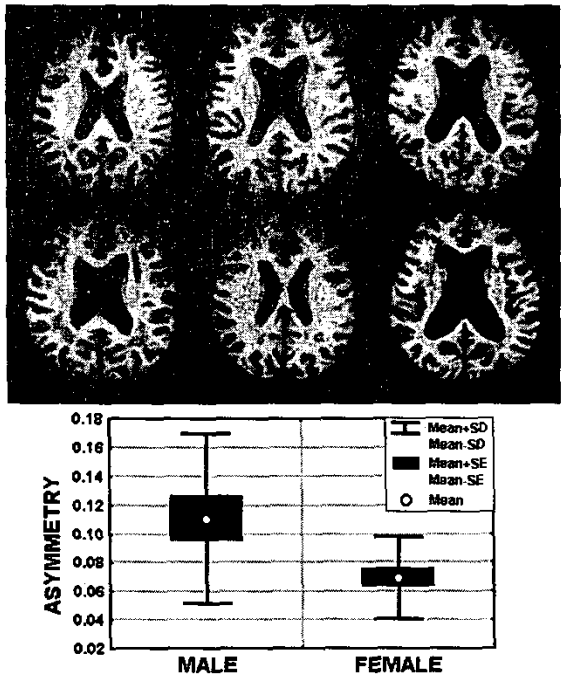

Figure 4. Gender-related asymmetry differences in healthy elderly subjects. Example slices of 3 male (top) and 3 female (middle) subjects and asymmetry evaluation results (bottom, N=33).

group and gender as two independent factors. As a result, there were no significant changes found associated with age (F=2.89, $p = 0.093$). This is perhaps because age-related changes manifest themselves differently for gray and white matter brain compartments. Thus, as a further investigation, all 55 brain images of group GR-AGING were segmented and asymmetry was measured for gray and white matters separately. Gray matter asymmetry was significantly greater in aged subgroup compared to young (0.096 vs. 0.075, F=21.43, $p < 10^{-6}$) while white matter asymmetry did not vary with age (F=1.29, $p = 0.258$).

4 Conclusion

Results reported with this study allow to draw the following conclusions:

(a) 3D volumetric texture analysis of anatomical MR images provides quantitative information about the brain structure in normal subjects and patients with pathological findings. It is sensitive enough to quantify differences associated with gender and normal aging.

(b) The analysis of inter-hemispheric brain asymmetry associated with gender revealed significantly higher asymmetry in males comparing females (mean value 0.145 against 0.101, t=7.23, $p < 10^{-6}$, N=210). The significance of this observation tends to decrease with age.

(c) There was no significant changes found in asymmetry degree with normal aging when considering brain tissue as a whole. Separate analysis of gray and white matters showed significant asymmetry increase with age (F=21.43, $p < 10^{-6}$) of gray but not white matter.

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