A New Method for Quantification of Age-Related Brain Changes

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Abstract

A new method is proposed for quantification of age-related brain changes. The method includes calculating 3D volumetric texture descriptors, extracting principal components, and assessing the significance of brain changes using multivariate analysis techniques. Structural changes were evaluated using high resolution anatomical MRI-T1 brain images of a group of 152 healthy subjects aged from 18 to 70 years (76 males and 76 females). The Talairach parcellation system was applied to study normal brain aging on four scale levels: the whole cerebrum, the nine coronal sections, the twelve axial sections, and 108 box-shaped sections resulting from both subdivisions. Statistical analysis has revealed significant brain deteriorations with age at different scale levels. Most of the brain regions are affected with a slight predominance in the frontal lobes. We concluded that 3D texture analysis followed by statistical evaluation procedures is a robust technique for detecting age-related changes in the anatomical MR images of the human brain.

Keywords: *brain, aging, 3D volumetric texture, co-occurrence*

1 Introduction

Macroscopic-anatomical descriptions of the human brain are acquired on conventional magnetic resonance (MR) scanners within minutes today. Age-induced degeneration and specific diseases of the central nervous system (CNS) cause macroscopic changes that may be revealed by MR imaging. A quantitative characterization of tissue changes may be gained from computer-based image analysis procedures in terms of shapes of structures, their tissue characteristics and pathological changes. Results of such an analysis are feature sets that may be linked in longitudinal and cross-sectional studies with clinical and cognitive data.

One of the crucial tasks here is to define what is considered as "normal" resp. "pathological". In comparison with the still valid gold standard - brain section - the digital analysis methods offer the advantage of studying large population groups at different ages and - in vivo. As a consequence, for a successful application of computer vision methods in a clinical setting, they have to be robust against varying scanner properties (i.e., changes in intensity, contrast and noise), and able to detect pathological changes at a well documented sensitivity level.

Recently, it was demonstrated that characterization of tissue properties by 3D volumetric texture analysis [3, 4] is robust and provides a high sensitivity for detecting image features that may be related to degeneration or attributed as signs of an CNS disease. This is the first work suggesting the use of volumetric texture analysis for quantification of small-scale brain tissue changes associated with normal aging. A rigorous statistical analysis in a reasonable large database detected significant changes with age. Extreme cases in terms of this statistic may be considered as pathological.

2 Materials and methods

Image data. Structural brain changes associated with age were studied in a group of 152 healthy subjects aged from 18 to 70 years (76 males, age 35.1 ± 13.4 years, and 76 females, mean age 36.1 ± 14.1 years). The age difference with gender was insignificant (p=0.650). Magnetic resonance imaging (MRI) was performed on a Bruker 3T Medspec 100 system, equipped with a bird cage quadrature coil, using a T1-weighted 3D MDEFT protocol [6]: FOV $220 \times 220 \times 192$ mm, matrix 256×256, 128 sagittal slices, voxel size 0.9×0.9 mm, 1.5 mm slice thickness, scanning time 15 min. Scan data were interpolated to an isotropical voxel size of 1.0 mm^3 using trilinear interpolation.

The outer hulls of the brain were removed and brains were aligned with the Talairach coordinate system [8] using an automated procedure [5]. The cerebrum image intensity was re-scaled to 0-255 by calculating the histogram and clipping 0.5% of voxels from both ends. Example slices of the brain images are given in Fig. 1.

Brain regions. Age-related changes were studied in the left and right brain hemispheres separately on four scale levels corresponding to the Talairach brain partitioning: the whole cerebrum, the nine coronal sections x1-x9, the twelve axial sections z1-z12, and 108 box-shaped sections resulting from both subdivisions.

Image analysis chain. At each scale level the following analysis chain was applied to every brain region: (a) computing extended co-occurrence image descriptors; (b) extracting principal components; (c) fitting a multivariate linear model to the data with age, gender, and brain region volume as three factors; (d) assessing the statistical significance of these factors using a multivariate analysis of variance (MANOVA) method with principal components as dependent variables; (e) deriving p-values for the age factor and correcting for multiple comparison associated with adjacent regions; (f) converting p-values to more convenient z-scores expressing statistical significance of age-related changes.

Co-occurrence image descriptors. We used extended multi-sort co-occurrence matrices suggested in [3] as structural descriptors of anatomical 3D MRI brain images. These descriptors are computed from elementary features of voxel pairs within a brain region and include intensity, intensity gradient magnitude, the angle between gradient vectors (orientation coherence/anisotropy), and the inter-voxel distance. The co-occurrence matrix of an image region is a multi-dimensional array. The matrix axes are associated with the above features and its elements represent the number of voxel pairs with certain feature values. All possible neighbors around each voxel with no repetition are considered for given distance range so that descriptors are rotation-invariant. Matrices are normalized for each distance bin separately. More formally, let us consider an arbitrary voxel pair (i,k) defined in 3D 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 extended six-dimensional co-occurrence matrix can be defined as:

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

where $g(i)\circ g(k)$ is the dot vector product and $g(i),\ g(k)$ are normalized intensity gradient vectors at voxel positions i and k. Gradient vector components were derived using a filter with the small $3\times3\times3$ window suggested in [9].

Implementation details. Following the experience of [4], the control parameters for co-occurrence descriptors were set to 8 intensity bins (32 units each), 8 gradient magnitude bins (115 gradient units each), 6 angle bins (30 degrees each), and the inter-voxel distance was set to one raster unit (i.e., an average neighborhood radius of 1.42 mm). The principal components were selected by the widely used Kaiser's criterion which retain only factors with eigenvalues greater than 1. The MANOVA method employed here is as described in [1] and implemented within the R statistical environment [7]. In all the analyses, except for the whole cerebrum, significance values were corrected for multiple comparisons using Holm's method [2]. Significance levels for two-tailed T-statistics were set to $p < 0.01$ what corresponds to $|z| > 2.58$.

The calculation of co-occurrence descriptors for MRI-T1 brain images was implemented in the C programming language. All the computations were done on a PC workstation with two Intel P-III 750 MHz processors and 1GB RAM running under the Linux operating system.

3 Results

Cerebral hemispheres. On a gross level of whole cerebral hemispheres the structural brain changes associated with age were highly significant with no specificity for the left and right hemispheres (p=7.1×10^{-21}, z=9.37 and p=7.3×10^{-21}, z=9.37 respectively). Number of principal components was also similar (11 and 10 respectively). A regression diagram plotting predicted age vs. real age is depicted on Fig. 2.

Talairach coronal and axial sections. The mean regional brain volume varied in coronal sections from 35 ml in section x1 to 314 ml in section x5 while among twelve axial slices it ranged from 12 ml in section z12 to 187 ml in section z9. In all the sections the age-related changes were well above the statistical significance threshold $|z| > 2.58$. The significance values for each section are plotted in Fig. 3.

Talairach corono-axial blocks. At this scale level both coronal and axial Talairach subdivisions were applied and structural changes in each block were assessed analogously. The number of principal components selected by the Kaiser criterion from co-occurrence descriptors is varied from 7 in the block x7z5 to 24 in the block x6z8, both in the left brain hemisphere. The color-coded significance maps are provided in Fig. 4.

4 Conclusions

Volumetric texture analysis followed by statistical evaluation proofed to be a robust technique for detecting age-related changes in MR images of the human brain. The main findings are:

- An increasing structural change at a small scale (millimeters), i.e., an increasing "graininess" is found predominately of the brain's white matter (see Fig. 1).
- This graininess is interpreted as an age-related deterioration of the highly structured white matter, i.e., by demyelinisation, an increasing number of small white matter lesions of vascular origin, and an growing extent of perivascular spaces (of Virchow-Robinson type).
- All white matter compartments are affected, with a slight predominance in the frontal lobes.
- Due to the high association of this measure with age it appears feasible to estimate the image-related age of a patient from her/his MRI data. A significant difference between the true biological age and the image-related age may be interpreted as a sign of pathological ageing.

Further studies are planned to define the microscopical nature of these brain texture changes.

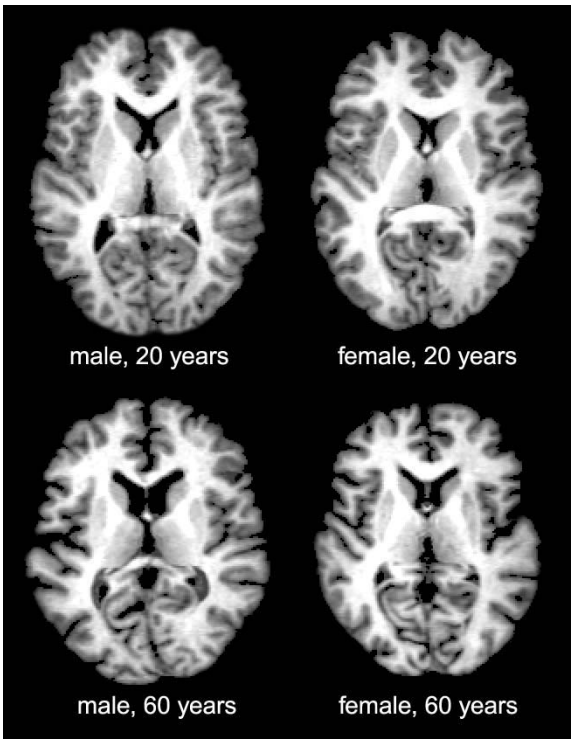

Figure 1. Example slices of MRI-T1 brain images of young and aged subjects.

Acknowledgments

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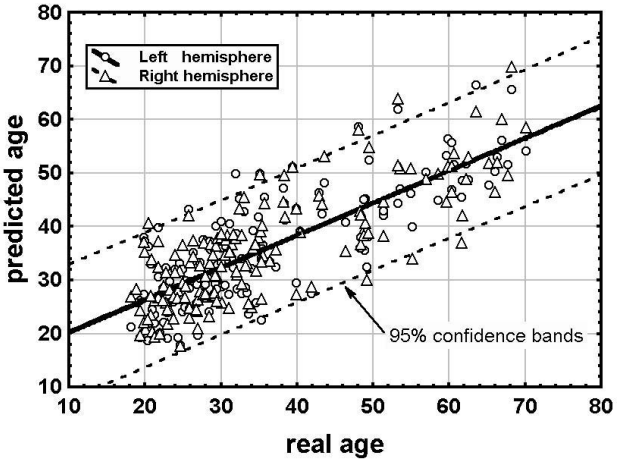

Figure 2. A regression diagram plotting the predicted age vs. real age for the left (circles) and right (triangles) brain hemispheres (152 subjects aged 18-70 years).

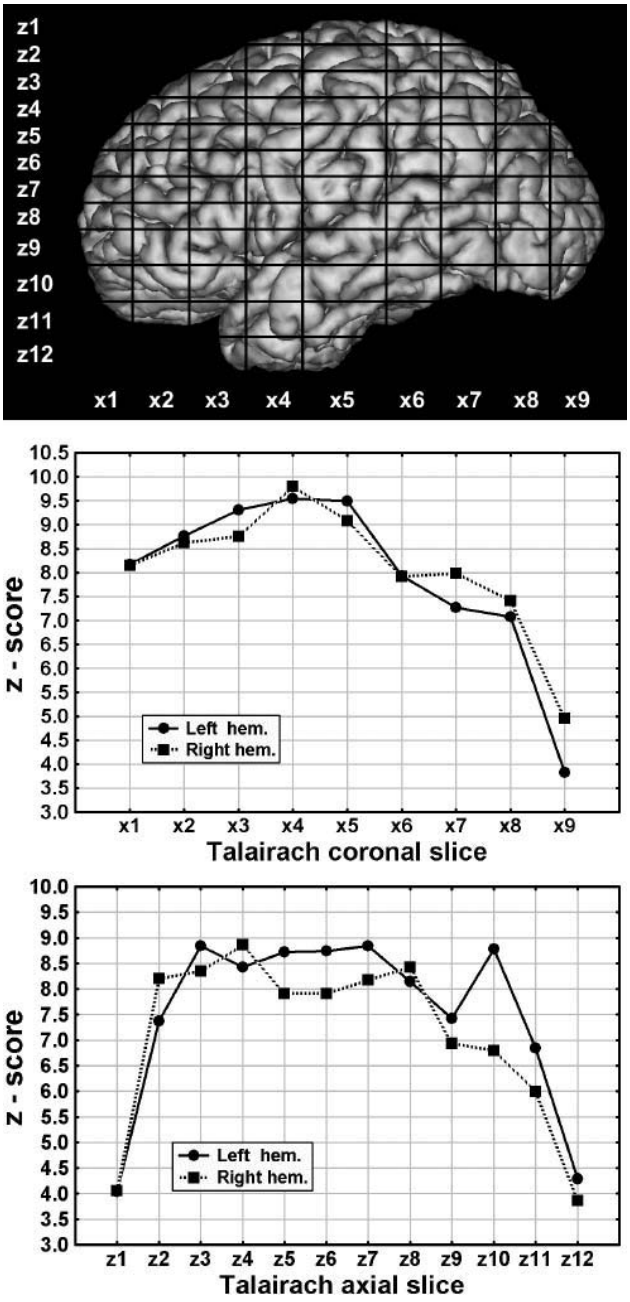

Figure 3. Talairach brain partitioning (top) and significance of age-related changes in coronal (middle) and axial (bottom) brain sections (152 subjects aged 18-70 years).

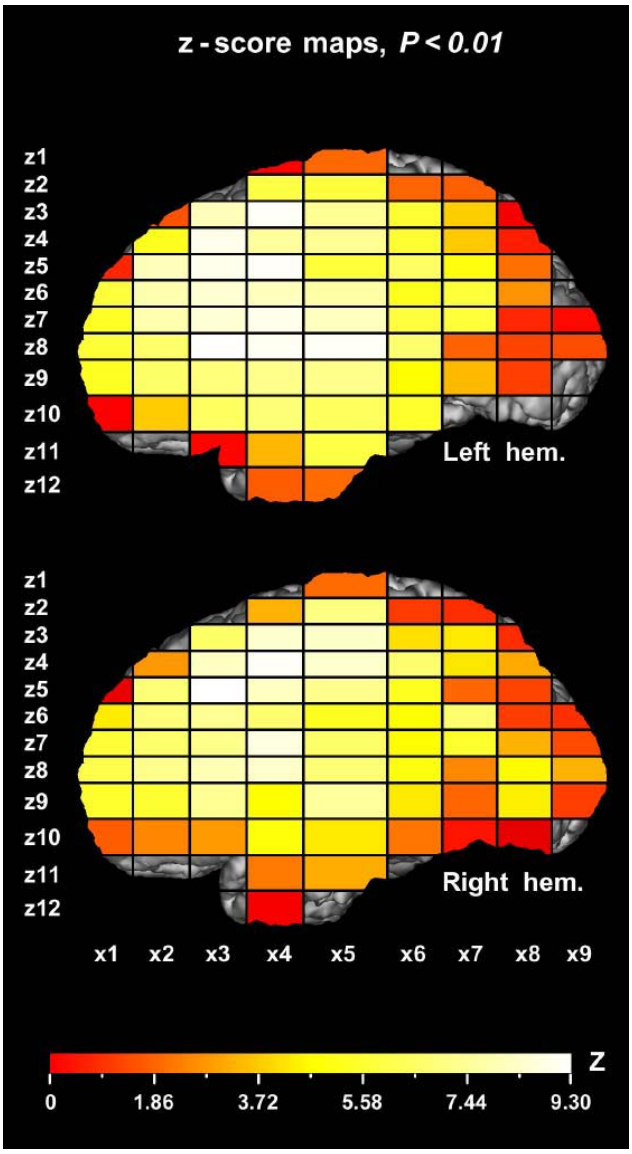

Figure 4. Significance of age-related brain changes in Talairach corono-axial blocks (152 subjects aged 18-70 years). Significance scores are coded using the color scale provided underneath.