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Comparison between healthy young and elderly individuals using MRI texture analysis

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Abstract

It is well known that the brain changes as we age. Several magnetic resonance imaging (MRI)-based studies have demonstrated structural changes in the brain, such as cortical thickness and volume. Conversely, few studies have investigated structural changes derived from MRI texture analysis. Texture analysis reflects underlying tissue characteristics, thus allowing the quantification of subtle structural variations in brain tissues that may not be apparent through standard image inspection. The aim of this study was to observe and compare brain texture in MRI images between healthy young and elderly individuals. To this end, MRI images from two groups, one of young and one of elderly individuals, were analyzed using the texture analysis technique with a second-order statistical approach, namely the gray-level co-occurrence matrix (GLCM). GLCMs computed in three dimensions were fitted to five intervoxel distances, and contrast and entropy parameters were extracted and compared between the groups. Statistically significant differences were found between the groups for both contrast and entropy parameters, for all intervoxel distances, suggesting that brain structure changes occur during aging. Analyzing the contrast and entropy values, respectively, for the young people (7.8 ± 4.5 and 1.7 ± 0.2) and the elderly groups (12.9 ± 6.1 and 2.0 ± 0.2), it is noted that the difference in parameters between the ages is more pronounced in the contrast. This indicates that the regions may exhibit greater local variations, such as reorganization and structural changes. This difference occurred between brain areas related to memory, reasoning, numerical processing, and language. This study analyzed two different groups of individuals; in the future, it would be interesting to conduct longitudinal studies evaluating the same individuals over time to corroborate these findings.

Keywords: aging; texture analysis; magnetic resonance imaging; gray-level co-occurrence matrix; contrast.

1. Introduction

The study of the human brain is a longstanding scientific endeavor, with investigations into its changes over life being equally well-established. However, a fundamental question remains unanswered: is there a universal pattern of brain changes that applies to all humans, or does this phenomenon vary significantly among individuals? Addressing this question requires examining both structural and functional changes in the brain, with aging serving as the main context for investigation.

One classical approach to understanding age-related brain changes involves post-mortem (PM) studies, wherein the brains of aging mammals are analyzed as models for the human brain. These studies focus on attributes such as neuron count and size, which are indicative of the brain's information-processing capacity. Findings from PM studies suggest that brain aging is heterochronic, that is, occurs at varying rates and times across different individuals and regions of the brain (1).

With the advent of advanced technologies, in vivo studies of the human brain using non-invasive imaging techniques, such as magnetic resonance imaging (MRI), have become increasingly feasible. Although in vivo approaches lack the histological precision of PM studies and involve uncertainties related to segmentation and pre-processing, they offer the advantage of directly observing human brain structures. Numerous studies using MRI data have highlighted the different effects of aging on gray and white matter. For instance, while white matter volume remains relatively stable with age, gray matter undergoes significant volumetric reduction (2).

Advanced MRI techniques, such as voxel-based morphometry (VBM), have further elucidated these changes. Studies revealed a linear decrease in global gray matter volume with age, with accelerated losses in regions such as the insula, superior parietal gyrus, central sulcus, and cingulate sulcus (3). Interestingly, certain regions, including the amygdala, hippocampus, and entorhinal cortex, exhibit minimal or no age-related changes (3).

Beyond volumetric analysis, texture analysis techniques have been employed to explore microstructural changes in brain tissue (4). These methods, based on the statistical distribution of gray levels in MR images, provide insights into the heterogeneity and symmetry of brain tissue (4). Studies have reported significant increases in asymmetry with age in regions like the inferior frontal gyrus and anterior cingulate, while decreases in asymmetry were observed in the optic radiation and angular gyrus (4).

In this context, the present study applied texture analysis to MR images to compare brain characteristics between two distinct age groups: younger and older adults. By correlating these findings with existing literature, this study aims to advance our understanding of age-related changes in brain tissue structure and inform future research directions.

2. Methods

2.1 Subjects

The data for this research were obtained from the OpenNeuro database (https://openneuro.org/), from the "Single Dose Intranasal Oxytocin Administration: Data from Healthy Younger and Older Adults" study (5). The images were obtained on a 3T Philips Achieva MRI Scanner with a 32-channel head coil. In this study, we used only the anatomical data, collected using a high-resolution three-dimensional T1w sequence: sagittal plane, TR/TE/TI = 7/3.2/2750 ms, flip angle = 8º; in-plane FOV = 240 mm x 240 mm; with imaging matrix 240 x 240; 170 contiguous sagittal slices with 1 mm slice thickness, 1x1x1 mm^3 isotropic voxels This comprised structural T1-weighted MR images of healthy adults that were separated into two different groups: one that included 41 young adults (48% female) with an age range of 18 to 31 years, and another that included 42 elderly adults (56% female) aged 63 to 81 years. None of the subjects had any neurological or psychiatric disorder, and all provided written consent before entering the study.

In this study, all of the women who were classified in the elderly group were post-menopausal, and all of the younger women were pre-menopausal.

2.2 Image processing

MR images were first normalized to a standard space using SPM12 (https://www.fil.ion.ucl.ac.uk/spm/software/spm12/). This spatially normalized images were used as the basis for all subsequent steps. Afterward, the images were anatomically segmented using the AAL atlas (6), creating 86 Regions of Interest (ROIs). Finally, the texture features were computed directly from these spatially normalized and segmented images. To calculate the GLCMs, the gray level of the images was normalized from 4096 to 256 to avoid overly sparse GLCMs (i.e., with many zero values) (6). Although the process of normalization can reduce the information contained in the GLCM and cause the loss of possible subtle differences between tissues, so the sparsity of the GLCM causes computational inefficiency and unstable texture features.

From the 86 AAL ROIs, 12 were chosen for analysis, namely: Amygdala, Angular gyrus, Anterior cingulate, Hippocampus, Insula, and Superior parietal gyrus, from the left and right hemispheres. These regions were selected based on findings related to age differences previously reported by Good et al. (3) and Kovalev et al. (4).

Direction-independent GLC matrices were then computed for each selected ROI, using MATLAB code developed in our group, which directly considers the 3D image (6). For each ROI, five GLCMs were calculated, one for each distance between voxels in the range from 1 to 5. Then, two parameters were extracted from each GLCM: contrast and entropy (7). Therefore, at the end of this process, we had 10 texture parameters per ROI, for each subject, for our analysis.

2.3 Texture analysis

Texture analysis is a technique that has been used in the field of medical image processing and can provide information about the brain and its characteristics (8). Texture can be considered as a group of image properties (e.g., smoothness, roughness) which can be used to compare different tissues in a given image, or even images from different groups, as is the case in this study.

Many approaches can be used to obtain texture parameters from digital images. In this study, we used the statistical approach based on the gray-level co-occurrence matrix (GLCM), which allows obtaining parameters that characterize stochastic properties of the spatial distribution of the gray levels of the image (7).

The GLCM is an N x N square matrix, with N being the number of gray levels available in the image (9). The (i,j) element of the GLCM represents the number of times that gray level i co-occurs with gray level j, given a distance d (in this case, 1 to 5 voxels) in a given direction (usually, horizontal, vertical, and both diagonals). However, in the present study, instead of calculating the matrices for 2D slices of the images, GLCMs were calculated directly for the 3D images. An isotropic GLCM was used, meaning that all directions were considered simultaneously. The (i,j) element of the 3D-GLCM represents the number of times that the reference voxel with gray level i co-occurs with a voxel with gray level j, located in the cubic shell centered in the reference voxel. The size of the cubic shell was also varied so that the intervoxel distance stayed in the (1,5) range.

2.3 Statistical analysis

First, a Mann-Whitney test was performed on the data from both groups (young and elderly) to evaluate the influence of sex in the texture parameters. Subsequently, a Mann-Whitney test comparing contrast and entropy among groups, joining all selected ROIs and GLCM distances, was performed. And finally, a Kruskal-Wallis test was applied to these parameters to compare both groups, separately for each distance and ROI. The significance level adopted was 0.05.

3. Results

After the data collection and processing phase, one participant was completely excluded from the analysis, and four ROIs were removed from another participant due to image rotation artifacts. The exclusion, criterion was that images with more than 0,2 rad rotation should be discarded. The brain texture data, obtained for the contrast and entropy parameters, were evaluated according to sex, age (young and elderly groups), ROIs, GLCM distances, and cerebral hemisphere.

Figure 1 shows the comparison between sexes for the contrast and entropy parameters, combining the groups (young and elderly), brain regions, and GLCM distances. This figure shows similar distributions among sexes for both texture parameters, indicating that this variable does not affect texture (as evaluated

in this study). Indeed, the Mann-Whitney test was non-significant for this comparison (p=0.414 for contrast and p=0.732 for entropy).

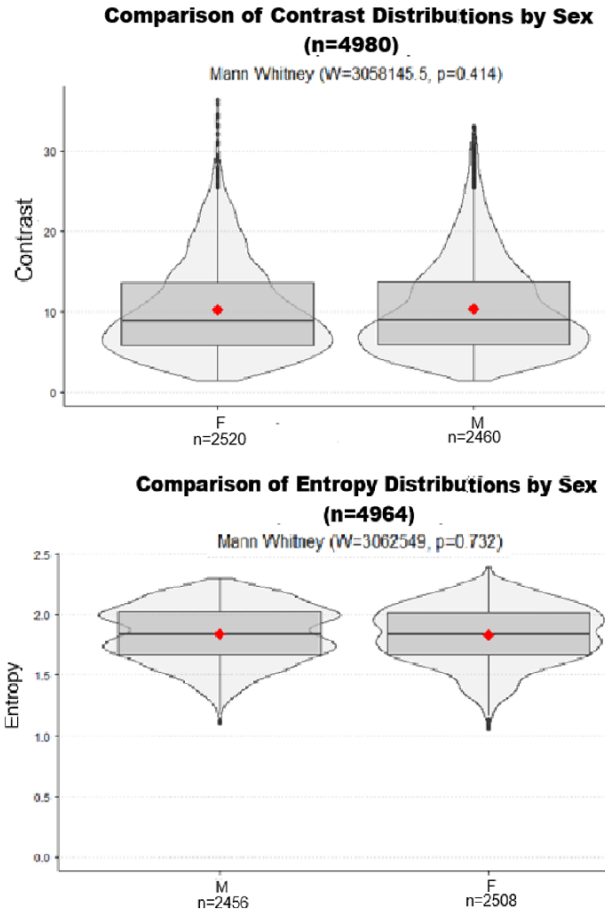

Figure 1. Distributions of contrast and entropy parameters by sex. Here, young and old individuals, all brain regions, and all distances of the GLCM were grouped, resulting in "n" observations

Figure 2 shows the comparison between the young and elderly groups, combining all brain regions and all GLCM distances. From these figures, a clear difference between the distributions of both groups can be seen, for both contrast and entropy, attested also by the Mann-Whitney test results (p<0.001 for both parameters). Also, both these parameters present a larger mean and median for the elderly group.

Finally, Figures 3 and 4 present the contrast and entropy distributions, respectively, for each group, separated by ROI, GLCM distance, and brain hemisphere (L = left, R = right). Both texture parameters show a clear separation between groups for all ROIs and GLCM distances. Contrast seems to present larger values as the GLCM distance is increased, while entropy distributions remain fairly the same across distances. The Kruskal-Wallis test was significant for the comparisons among groups for all ROIs and distances (p<0.001).

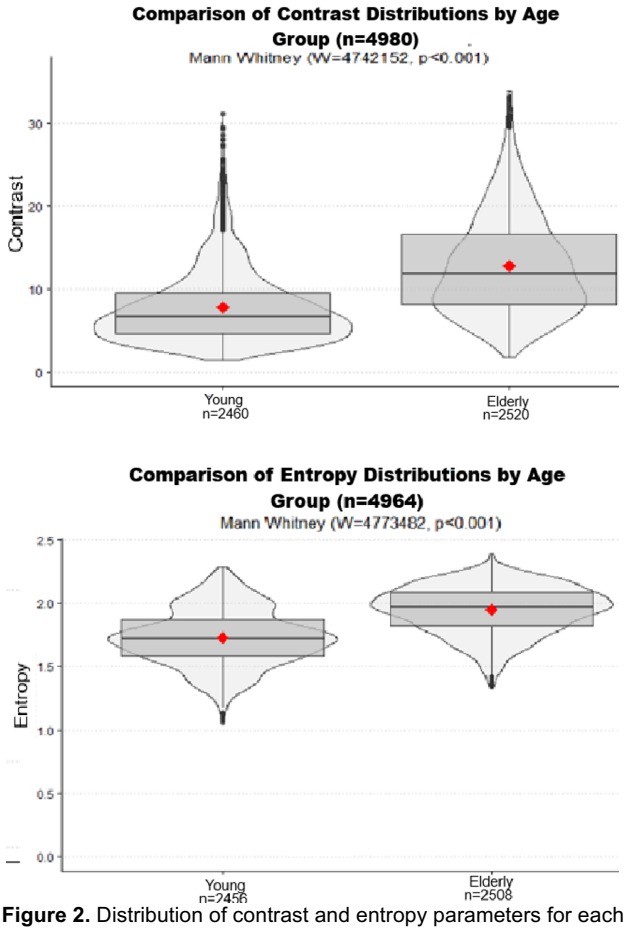

Figure 2. Distribution of contrast and entropy parameters for each studied group (young and elderly). Here, all brain regions and all GLCM distances were grouped, resulting in "n" observations.

4. Discussion

Regarding the influence of sex on the results, we found that the sex distribution is homogeneous across age groups and, therefore, this variable is not expected to affect the subsequent findings. This lack of significant sex differences in texture parameters introduces a contrast with well-established macrostructural studies of brain aging, as those consistently demonstrate that cortical thinning and brain atrophy trajectories exhibit a significant sex influence, where healthy aging males usually experience more cortical thickness reduction and accelerated volume loss compared to females (10). However, while traditional voxel-based morphometry (VBM) or cortical thickness measurements evaluate macroscopic boundaries, GLCM texture analysis captures microstructural alterations and gray-level distribution, so our findings suggest that the subtle microstructural reorganization of brain tissue assessed by contrast and entropy operates independently of anatomical gender disparities. It is also important to acknowledge that spatial normalization to a standard space can be responsible to smooth the image and reduce the information in the GLCM, because of the process of interpolation needed to normalize the images into the standard space, recalculating the position and gray level. However, since the GLCM parameters evaluate local statistics (small distance, 1 to 5 voxels), and the SPM12 algorithm applies a global transformation,

possibly the local impact does not eliminate the intrinsic characteristics of the tissue.

A significant difference in contrast was identified between the age groups (Figure 2 – top – and Figure 3), with older participants showing higher contrast values than the younger ones. Higher contrast values indicate greater local variation in gray levels within the image (9), which may suggest that structural changes or reorganization occurred in the examined brain regions over time.

Regarding the entropy parameter, a similar pattern was observed. Significant differences were found between the age groups, with the elderly group also presenting higher entropy values compared to the younger group. Entropy measures the level of disorder in the gray-level distribution of an image (9), which may reflect tissue reorganization leading to increased heterogeneity.

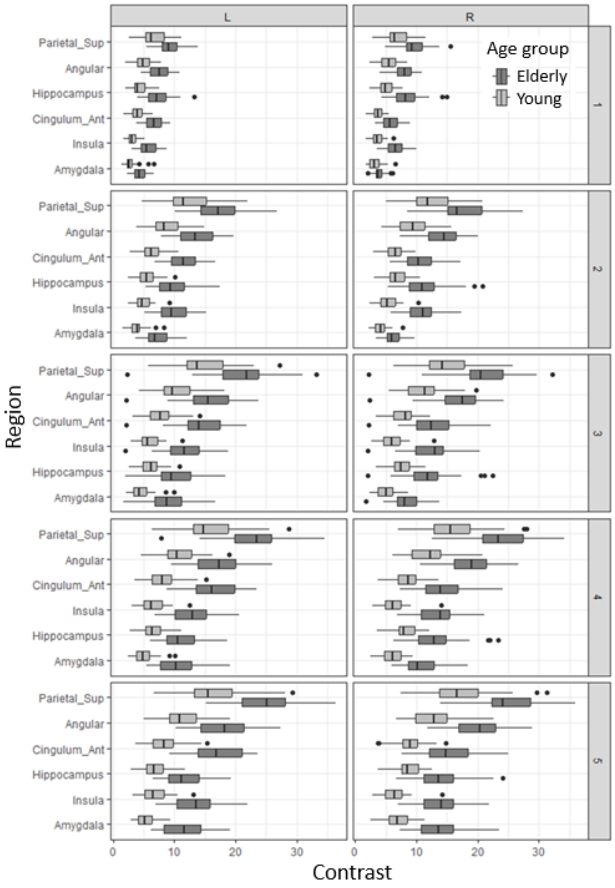

Figure 3. Contrast for each group, separated by brain region and GLCM distance. The left column refers to the regions of the left hemisphere and the right column to the regions of the right hemisphere.

When analyzing the brain structures that exhibited age-related changes, it is notable that they are primarily located in regions associated with memory (e.g., Amygdala, Angular Gyrus, and Hippocampus) (11,12), language and numerical processing (e.g., Angular Gyrus and Insula) (11), and emotional regulation (e.g., Amygdala and Anterior Cingulate Cortex) (12). According to the literature, cognitive abilities that tend to decline more noticeably with aging include episodic memory—which refers to the long-term memory of specific experiences and events, including temporal and spatial details—processing speed, reasoning (12), and spatial visualization (13). In this case, the cognitive functions that present a greater decline are directly related to the regions in which we found a greater change in the contrast and entropy parameters studied.

Our results corroborate findings by other studies (3,4). Indeed, using texture analysis based on the 3D texture analysis method, Kovalev et al. found brain asymmetries in the inferior frontal gyrus, insula, and anterior cingulate (4). Also, Good et al. used voxel-based morphometry to compare young and older adults, and found that global grey matter volume decreased linearly with age - the insula, superior parietal gyrus, and cingulate sulcus displayed accelerated loss (3). Notably, the brain regions highlighted in those studies also exhibited significant variations in contrast and entropy parameters in the present investigation. It is important to highlight that recent and significant studies use texture to try to identify diseases such as Alzheimer's or SNAP (Suspicious Non-Alzheimer's Pathophysiology) early on (17,18). These studies show that brain texture changes even before volume decreases. However, most of them focus only on patients with the disease (or at risk of developing the disease) and analyze the data using fixed distances (usually only 1 voxel) or techniques that mix various metrics into abstract components. The difference in our work is that we focus strictly on healthy aging, comparing young and elderly individuals without any pathology. Furthermore, instead of using abstract metrics, we analyzed pure Contrast and Entropy, varying the distance between voxels from 1 to 5. This allowed us to discover that, in relation to aging, contrast increases very clearly as the distance between voxels grows.

This study has some limitations. The MR images used had to be normalized to a much smaller number of gray levels (from 4096 to 256) in order not to produce sparse GLCMs, which leads to some loss of information. Despite this, significant differences among groups were found. Nevertheless, in future studies, other texture analysis methods may be explored, such as the run-length matrix (14), binary patterns (15), or wavelets (16). Also, the assessed groups were composed of different individuals. It would have been interesting to have the same individuals evaluated over time, to see if the changes are the same found here. Finally, a larger sample would help to increase the robustness of the results.

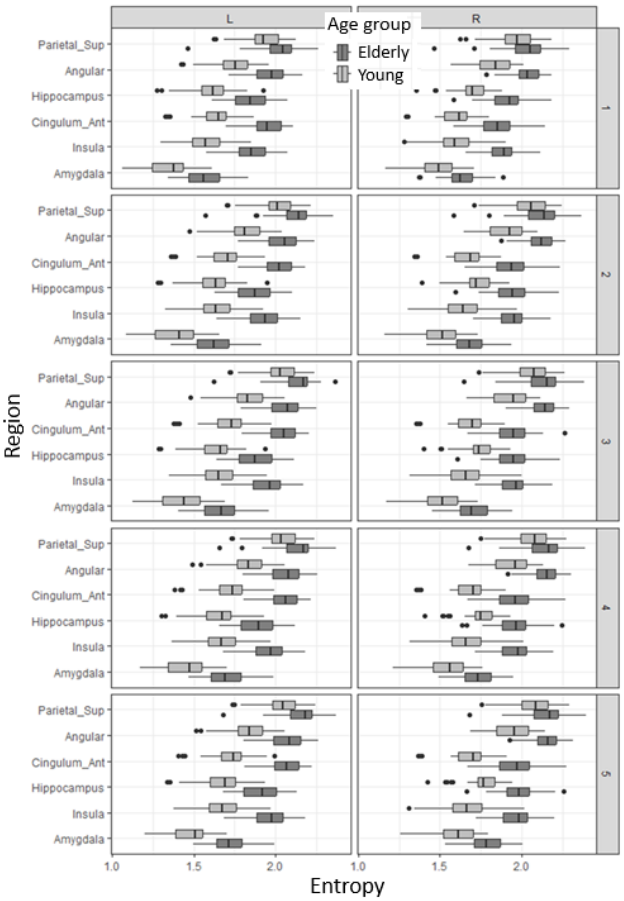

Figure 4. Entropy for each group, separated by brain region and GLCM distance. The left column refers to the regions of the left hemisphere and the right column to the regions of the right hemisphere.

5. Conclusions

Based on the results and the preceding discussion, it is reasonable to assert that texture analysis successfully identified age-related changes in brain organization, corroborating findings reported by other studies (3,4). These parameters respectively quantify the local variation in gray levels within MRI images (contrast) and the degree of disorder in gray-level distribution (entropy). Considering that texture analysis is primarily employed to detect microstructural tissue changes, the observed variations may indicate a reorganization of the anatomical regions analyzed.

According to the literature, various cognitive functions, including memory, reasoning, and information processing, tend to decline with age, as discussed by Salthouse (13). Given that these cognitive abilities are closely linked to the proper functioning and integration of the brain regions examined in this study, it is plausible that such cognitive decline is related to structural alterations that occur in these areas over time.

In conclusion, the findings support the use of texture analysis as a valid technique for investigating brain aging. This method holds potential as a valuable tool for identifying structural changes that may be associated with cognitive decline and age-related neurological conditions. Furthermore, the present study aligns with previous research and contributes to the growing body of knowledge concerning the structural and functional changes in the human brain across the lifespan.

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