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ORIGINAL ARTICLE

Volumetric of the lateral ventricles in computed tomography images in Cubans adults with normal cognitive functions

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Abstract

Introduction: The use of morphometric methods based on neuroimaging to determine brain volumetric related to aging for clinical diagnosis has been largely restricted to high-resolution imaging techniques. Texture, as a method of image analysis, has shown promising results in the detection of visible and non-visible lesions, and that in computerized axial tomography studies they are scarce. **Objective:** The objective of the study was to evaluate the effect of normal aging on the volume of the lateral ventricles, estimated from single-slice computed tomography (CT) imaging techniques, using an automatic processing method of homogeneous texture indices. **Methodology:** An observational and analytical study was developed in 320 subjects with normal neurocognitive functions and neuropsychiatric examination, aged between 30 and 75 years and over, who underwent a single-slice Computed Axial Tomography of the skull. An image segmentation method based on homogeneity was used. **Results:** The analysis of variance showed that advancing age is associated with a proportional increase in the volume of the lateral ventricles. **Conclusions:** The morphometric method of the lateral ventricles developed from CT/homogeneity segmentation images, allows to quantify the cerebral volumetric changes associated with normal aging and can be used as a biomarker of cerebral atrophy.

Keywords: Ventricular volumetric. Computed tomography. Normal cognitive functions.

Volumetría de los ventrículos laterales en imágenes de tomografía computarizada en adultos cubanos con funciones cognitivas normales

Resumen

Introducción: El empleo de los métodos morfométricos a partir de neuroimágenes, para determinar la volumetría cerebral relacionada con el envejecimiento para el diagnóstico clínico, han sido restringidos en su gran mayoría, a técnicas de imágenes de alta resolución. La textura, como método de análisis en imágenes, ha mostrado prometedores resultados en la detección de lesiones visibles y no visibles, y en que en los estudios por tomografía axial computarizada (TAC) son escasos. Objetivo: Evaluar el efecto del envejecimiento normal en el volumen de los ventrículos laterales, estimado a partir de técnicas de imágenes de tomografía computarizada monocorte, empleando un método de procesamiento automático de índices de texturas

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homogéneas. **Metodología:** Se desarrolló un estudio observacional y analítico, en 320 sujetos con funciones neurocognitivas y examen neuropsiquiátrico normales, en edades comprendidas entre 30 y 75 años y más, a los que se le realizó una Tomografía Axial Computarizada de cráneo monocorte. Se empleó un método de segmentación de imagen basado en la homogeneidad. **Resultados:** El análisis de varianza demostró que el avance de la edad se asocia con un incremento proporcional del volumen de los ventrículos laterales. **Conclusiones:** El método de morfometría de los ventrículos laterales desarrollado a partir de imágenes de Tomografía Computarizada/Segmentación por homogeneidad, permite cuantificar los cambios volumétricos cerebrales asociados al envejecimiento normal y puede ser utilizado como un biomarcador de atrofia cerebral.

Palabras claves: Volumetría ventricular. Tomografía computarizada. Funciones cognitivas normales.

Introduction

Neural aging is accompanied by structural and functional transformations in the nervous system¹⁻⁴. Therefore, to characterize brain morphology and its association with age- and sex-related development, function, and neurodegenerative processes in healthy humans, as well as local morphological alterations found in psychiatric disorders and neurological diseases is crucial for the development of modern neuroscience⁵⁻⁷. This fact becomes more relevant if one takes into account that more and more people reach more advanced stages of life, where the risk of suffering from neurodegenerative diseases⁴. These represent a serious health problem and there are still obstacles that hinder their correct differentiation^{2,3}.

In recent years, efforts have focused on the development of segmentation methods for computed tomography (CT) images^{4,8}, but often a large number of features are involved, many of which are redundant or irrelevant. The selection of attributes or selection of characteristics seeks to solve the problem of the dimensionality of the information⁸. Within the framework of this study, a texture analysis is delivered under the category of recognition of homogeneity patterns, in a way that is sufficiently appropriate to discriminate to which class it belongs.

In our environment, although CT is widely used in the clinical setting, automatic segmentation methods are not available to estimate ventricular volume. Due to the above, the present work is carried out to determine the volumetric of the lateral ventricles and to identify the effect of age on these structures and its possible use as a quantitative biomarker of cerebral atrophy, through an automatic processing of texture indices homogeneous.

Materials and methods

Type of study

An observational and analytical study of clinical cases was developed.

Population

The population consisted of 320 patients, including 160 men, grouped in the age ranges of 34 years and under (1.9%), 35-44 (23.1%), 45-54 (25.0%), 55-64 (25.0%), 65-74 (19.7%), and 75 and over years (5.3%) who presented normal neurocognitive functions, evaluated through the mini mental status examination. The volunteers included presented a previous indication for head CT and attended the imaging service of the Saturnino Lora Torres Hospital. Their results were reported as negative for the presence of any old or recent disease of ischemic or vascular origin, or any structural brain alteration. Patients with a confirmed diagnosis of neurological and psychiatric diseases, a history of traumatic brain injury due to accidents, the presence of risk factors that have a known effect on the brain structure in the course of degenerative diseases, family-type neurocognitive disorders, schizophrenic disorders were excluded, pregnancy, as well as the presence of cognitive impairment.

Bioethical considerations

Authorization was requested and approved by the scientific council of the institution and by the ethics committee of each health institution involved in the development of the research. Participation in the study was carried out under the principle of voluntariness. The volunteers received prior clinical indication for a head CT, in the absence of neuropsychiatric manifestations. We accepted the ethical principles for research in human beings, this under the Declaration of Helsinki in force in Cuba.

Data processing and analysis

Ventricular volumetric reconstruction was obtained from a segmentation method based on the analysis of homogeneous textures and the Bicubic interpolation



Figure 1. Image pre-processing to reduce the noise level. The image on the right shows a tomography slice of a simple skull. The image in the center is the result of the application of anisotropic diffusion filters. The image on the left is the result of applying homogeneity-based segmentation during the pre-processing stage.

Source: Collection of images in DICOM format from the Imaging Department of the Saturnino Lora Torres Provincial Hospital.

technique, using the gray level co-occurrence matrix (GLCM), also known as the gray level spatial dependence matrix.

Assessment instrument (of global cognitive functioning)

All the volunteers were given the mini mental status exam (MEEM) standardized and approved for the Cuban population⁶.

CT technique procedure

The CT scanner used in this study was SIEMENS, single slice. Each patient had between 18 and 22 cuts with a thickness of 5 mm in this study. The size of the matrix of each segment was 512×512 pixels and the pixel size was 0.426 mm with a gray level of 16 bits.

Morphometric estimation method of the cerebral ventricle

In this study, the technological tool iMagis, indigenous to Cuba and certified for use by the National Center for the Registration of Medical Equipment of the Cuban Ministry of Public Health, was used. Widely spread and used in radiology services in the country⁹, with a more updated version called NeuroiMagis, which allows three-dimensional reconstructions and morphometric calculations through the recognition of homogeneity patterns through texture analysis. For morphometric estimates, an interactive segmentation method with three phases was implemented: pre-processing, feature extraction, and feature selection.

Pre-processing

The initial stage was the conversion of the image to a gray scale level. In the second step, the existence of noise and artifacts in the image was eliminated using the anisotropic diffusion filtering technique^{10,11} (Fig. 1).

Feature extraction

Automatic texture feature extraction was performed, based on the GLCM, where the image was automatically divided into K clusters by estimating features of homogeneity obtained from a Co-Occurrence matrix^{12,13} (Fig. 2).

It is not necessary to use the window configuration of the classic GLCM approach, all the variability information is obtained from the complete image.

Thanks to the weight factor (1 + (i - j) 2) - 1 where i and j describe the intensity values of the ensemble, the homogeneity index obtains small contributions from non-homogeneous combinations observed at the intensity points relative to each other. The result is a low homogeneity index value for non-homogeneous regions and a relatively higher value for homogeneous regions.



Figure 2. Recognition of homogeneity patterns through texture analysis in tomography slices at different levels of the brain.

Feature selection

The region of interest was segmented by combining texture information with the region growth approach. Finally, to evaluate the accuracy of the proposed approach, the Dice coefficient similarity metric was used¹⁴⁻¹⁶ (Fig. 3).

The Dice coefficient measures the degree of similarity between sets, regardless of the type of elements. It is a normalized value that reaches values close to one when the coincidence is great and close to zero when the coincidence between the segmented region and the real one is little. In this investigation, a value of 0.96 was achieved.

Statistic analysis

The volumetric measurements were grouped according to the age group to which the subjects studied belonged and were summarized through the arithmetic mean and standard deviation. Intervals for the mean of 95% confidence were estimated. To identify the possible differences between the age and gender groups, the possible correlation between the dependent variables that measure volumetric was first identified. As there was a very high correlation that denotes multicollinearity, the use of multivariate analysis of variance (ANOVA) was discarded and it was preferred to carry out an ANOVA of a separate factor for each dependent variable. Minitab[®] 19.2 (64-bit) was used as statistical processor.

Results

During the analyzed period, the population consisted of 320 patients who expressed their willingness to participate in the study, of which 50.0% were men, grouped in the age range of 30-75 years and over. 100% of the volunteers presented a previous indication for a cranial CT



Figure 3. Segmentation of the different parts of the lateral ventricles in the tomography slices at different levels of the brain.

scan, in the imaging service of the Saturnino Lora Torres Hospital and whose results were negative; they presented normal neurocognitive functions, neuropsychiatric evaluations and negative physical examinations. 17 (36.2%) patients were excluded from this investigation, 10.6% for presenting cognitive impairment, 4.3% with positive neuropsychiatric evaluation, and 21.3% of the volunteers presented positive signs at the time of the neurological system examination.

In relation to the variables analyzed, table 1 shows the values of the mean, standard deviation and the confidence intervals of the volume of the lateral ventricles for each of the age groups. The applied statistical analysis, one-way ANOVA, confirmed that the grouped ages in the selected groups have a significant effect on the total volumetric of the lateral ventricles and on the right and left ventricular volumetric. The comparison of the mean values showed that age has a linear relationship with the total volume of the lateral ventricles. This behavior is also true for the right and left ventricles. The *posteriori* comparative analysis, which is evidenced in table 2, reveals the effect of the ages included in the different age groups on the total and right and left volumetric of the lateral ventricles.

Discussion

In routine clinical practice, it is shown that the existing morphometric techniques have not been able to prevail, in part due to the inaccessibility of technical methods, to which is added their high cost and their known limitations to low-resolution images³. Due to the absence of morphometric patterns that characterize the study population in the present study, a morphometric quantification method has been developed that includes segmentation of CT images that allow the identification of informative characteristics of a massive set of original characteristics in pre-clinical stages and volumetric calculations which using single-cut CT images, a technique that exists in low-income countries, it has

Volume (mm³)	Age groups (years)	n	Mean	Standard deviation	Confidence interval for the mean at 95%		F	Sig.
					Lower limit	Upper limit		
Total ventricular volume	30-34	6	13078,950	4611,936	8239,019	17918,881	20,294	0.000
	35-44	74	15343,951	6918,675	13741,024	16946,878		
	45-54	80	17775,595	9492,683	15663,102	19888,088		
	55-64	80	22659,375	10947,326	20223,167	25095,583		
	65-74	63	30622,462	16176,855	26548,374	34696,550		
	75 and over	17	38261,735	22556,541	26664,232	49859,239		
	Total	320	21963,713	13593,987	20468,611	23458,815		
Right lateral ventricle volume	30-34	6	6353,100	3118,846	3080,071	9626,129	16,979	0.000
	35-44	74	7699,097	3836,557	6810,239	8587,956		
	45-54	80	8620,286	5020,891	7502,942	9737,631		
	55-64	80	10933,654	5766,935	9650,285	12217,022		
	65-74	63	14529,919	7624,182	12609,794	16450,044		
	75 and over	17	18411,535	11137,978	12684,915	24138,155		
	Total	320	10626,713	6717,387	9887,917	11365,508		
Left lateral	30-34	6	6725,850	3115,113	3456,739	9994,961	18,314	0.000
ventricle volume	35-44	74	7644,854	3743,307	6777,600	8512,108		
	45-54	80	9155,309	4903,864	8064,007	10246,610		
	55-64	80	11725,727	5822,659	10429,958	13021,497		
	65-74	63	16092,543	10054,891	13560,251	18624,834		
	75 and over	17	19850,200	12339,580	13505,773	26194,627		
	Total	320	11337,003	7623,610	10498,538	12175,467		

Table 1. Summary measures and effect of age on the right and left lateral and ventricular total volumetric

been possible to quantify these results, obtaining a morphometric pattern that describes the increase in the volume of the ventricles with respect to age and its possible use as a biomarker of brain atrophy.

Knowledge of the anatomy of the ventricular system is essential for clinicians, neurosurgeons, and radiologists^{17,18}. Normal reference values of the ventricles, regardless of the type of study used, are necessary to obtain reference data to interpret pathological changes, plan surgery, and determine the presence and progress of some neurological diseases^{18,19}.

The assessment of the increase in the ventricular system is frequently done qualitatively, based on the simple visual analysis of the tomography study; it can also be done quantitatively based on the Evans ventricular index (IE), which must be > 0.3 millimeters (mm)^{3,4}.

Shaikh Shamama¹⁸, morph metrically analyzed the width of the frontal horns of the lateral ventricles. The results showed that these structures gradually increased in size from the age group of 30-39 years and their maximum values were described in the group of 70-79 years. These results are somewhat similar to ours, since the ventricular increase was evident in the 35-44 group, accentuating it in the 64-75 and 75 and older groups. Polat and coauthors¹⁹ studied the ventricular system in healthy Turkish subjects, reporting statistically significant results for the older age groups. Dzefi Tettey²⁰, when determining the Evans index and the effect of age on this index, demonstrated the effect of age, obtaining the highest values in the age groups between 62-71 and 72 years and over.

It is worth emphasizing, as has been shown, that most authors have studied the morphometrics of the lateral

Volume (mm³)	(I) Age groups (years)	(J) Age groups (years)	Mean difference (I-J)	Typical error	Significant	Confidence interval for the mean at 95%	
					-	Lower limit	Upper limit
Total lateral	34 and under	65-74	-17543,5119*	5089,218	0.039	-34585,711	-501,313
volume		75 and over	-25182,785*	5656,349	0.002	-44124,131	-6241,440
	35-44	55-64	-7315,423*	1921,197	0.014	-13748,912	-881,936
		65-74	-15278,510*	2041,956	0.000	-22116,385	-8440,636
		75 and over	-22917,783*	3203,707	0.000	-33645,996	-12189,571
	45-54	65-74	-12846,866*	2006,435	0.000	-19565,791	-6127,943
		75 and over	-20486,140*	3181,184	0.000	-31138,931	-9833,349
	55 a 64	35-44	7315,423*	1921,197	0.014	881,936	13748,912
		65-74	-7963,086*	2006,435	0.009	-14682,011	-1244,163
		75 and over	-15602,360*	3181,184	0.000	-26255,151	-4949,569
	65 a 74	34 and under	17543,511*	5089,218	0.039	501,313	34585,711
		35 a 44	15278,510*	2041,956	0.000	8440,636	22116,385
		45 a 54	12846,866*	2006,435	0.000	6127,943	19565,791
	75 and over	34 and under	25182,785*	5656,349	0.002	6241,440	44124,131
		35 a 44	22917,783*	3203,707	0.000	12189,571	33645,996
		45 a 54	20486,140*	3181,184	0.000	9833,349	31138,931
		55 a 64	15602,360*	3181,184	0.000	4949,569	26255,151
Right lateral	34 and under	75 and over	-12058,435*	2852,528	0.004	-21610,662	-2506,208
volume	35-44	65-74	-6830,821*	1029,770	0.000	-10279,200	-3382,443
		75 and over	-10712,438*	1615,647	0.000	-16122,736	-5302,140
	45-54	65-74	-5909,632*	1011,856	0.000	-9298,024	-2521,242
		75 and over	-9791,249*	1604,289	0.000	-15163,511	-4418,987
	55-64	65-74	-3596,265*	1011,856	0.029	-6984,656	-207,874
		75 and over	-7477,881*	1604,289	0.001	-12850,144	-2105,619
	65-74	35-44	6830,821*	1029,770	0.000	3382,443	10279,200
		45-54	5909,632*	1011,856	0.000	2521,242	9298,024
		55-64	3596,265*	1011,856	0.029	207,874	6984,656
	75 and over	34 and under	12058,435*	2852,528	0.004	2506,208	21610,662
		35-44	10712,438*	1615,647	0.000	5302,140	16122,736
		45-54	9791,249*	1604,289	0.000	4418,987	15163,511
		55-64	7477,881*	1604,289	0.001	2105,619	12850,144
Left lateral ventricle volume	34 and under	75 and over	-13124,350*	3210,602	0.006	-23875,652	-2373,048

Table 2. Age groups with significant differences according to the *posteriori* multiple comparison tests

(Continues)

Volume (mm³)	(I) Age groups (years)	(J) Age groups (years)	Mean difference (I-J)	Typical error	Significant	Confidence interval for the mean at 95%	
						Lower limit	Upper limit
	35-44	55-64	-4080,873*	1090,491	0.017	-7732,587	-429,160
		65-74	-8447,688*	1159,035	0.000	-12328,937	-4566,441
		75 and over	-12205,345*	1818,456	0.000	-18294,789	-6115,903
	45-54	65-74	-6937,234*	1138,873	0.000	-10750,964	-3123,504
		75 and over	-10694,891*	1805,672	0.000	-16741,525	-4648,258
	55-64	35-44	4080,873*	1090,491	0.017	429,160	7732,587
		65-74	-4366,815*	1138,873	0.013	-8180,546	-553,085
		75 and over	-8124,472*	1805,672	0.001	-14171,106	-2077,839
	65-74	35-44	8447,688*	1159,035	0.000	4566,441	12328,937
		45-54	6937,234*	1138,873	0.000	3123,504	10750,964
		55-64	4366,815*	1138,873	0.013	553,085	8180,546
	75 and over	34 and under	13124,350*	3210,602	0.006	2373,048	23875,652
		35-44	12205,345*	1818,456	0.000	6115,903	18294,789
		45-54	10694,891*	1805,672	0.000	4648,258	16741,525
		55-64	8124,472*	1805,672	0.001	2077,839	14171,106

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*The mean difference is significant at the 0.05 level.

ventricles according to their different parts through linear measurements, not finding robust scientific evidence showing the morphometric results of the study of these structures together. We are of the opinion that obtaining the Evans ventricular index and others, such as the indices of the frontal, occipital, fronto-occipital, bicaudate, Huckman, and others horns, take a long time, require specialized software and the evaluator's expertise in the knowledge of the Anatomy of the central nervous system.

Taking into account that volumetric studies are widely used today and recommended due to the reliability of the results and the shorter time needed for their determination, the quantification of the encephalic ventricular system was carried out by its volumetry, using an approach to recognize patterns of intensities in an image dataset for interactive segmentation.

For the quantitative evaluation of the regions of interest, we show the results of the automatic extraction of homogeneous features in artificial images (Fig. 4). The original images (4A and 4C) and the colors in the images (4B and 4D) represent the classes of the segmented patterns. The numerical values in (4B and 4D) represent the value of the homogeneity index of each class. Figures 4B and 4D show the satisfactory results in the segmentation of intensity patterns proposed in the artificial images when they coincide with the number of referenced classes. What is expected is to obtain emission signals with a high homogeneity value between their adjacent pixels without falling into over-segmentation.

By means of a visual identification it can be observed how the classes in the segmented image are well preserved by the method. The numerical values in images 4B and 4D indicate an estimate of the homogeneity in the area of the classes.

The fact that the proposed method is sensitive to noise is also visually evident in these results by the distortion between the regions. However, the characteristic of textures in CT images could lead to interesting directions for future research.

There are very few studies where methods are applied with which our approach can be quantitatively compared.



Figure 4. Segmentation of intensity patterns in original and artificial images (prepared by the authors). A and C: are a representation of artificial images, which were created with a high rate of homogeneity between classes. B and D: show the satisfactory results in the segmentation of intensity patterns proposed in the artificial images when coinciding with the number of referenced classes. The colors in the images represent the classes of the segmented patterns. The numerical values represent the value of the homogeneity index of each class.

Deleo and co-authors²¹ proposed a semi-automated method. Users were asked to manually select representative points of cerebrospinal fluid, gray matter, and white matter in the region superior to the third ventricle to avoid artifacts. The thresholds were calculated based on the manual specification of the aforementioned structures. Its drawbacks include: manual specification, which is tedious and error-prone without prior training, and spatial information is not exploited to treat tissues that have overlapping intensity.

Soltanian-Zadeh and Windham¹⁴ proposed finding brain contours semi-automatically, manually specifying thresholds in different regions to binarize CT slices, using edge tracking to find contours, employing multi-resolution to resolve broken contours, and specify seed points to collect the desired contour. The large amount of user intervention is its main drawback.

However, recent advances in CT scanner technology and improvement in CT image quality suggest that the ability to distinguish soft tissue types by this diagnostic means is becoming more feasible.

In contrast, Kemmling and co-authors²² introduced a probabilistic atlas based on pre-segmented MRI volumes that were co-registered with CT images to perform tissue classification, but no validation or quantitative approach to this approach was found implemented in your study.

More recently, Manniesing²³ proposed a method for CT-based segmentation that requires manual corrections using dedicated software and is also based on the average of CT volumes acquired longitudinally of the same subject after administration of a cellular agent. Contrast to improve the contrast-to-noise ratio from image.

The accuracy of our approach in the setting where more than one CT scan is not available is unknown. Furthermore, averaging CT volumes acquired longitudinally can produce undesirable results in cases where the evolution of pathology between time points modifies the shape and structure of the brain. In addition, the Manniesing method involves the segmentation of gray and white matter and cerebrospinal fluid through contrast-enhanced CT.

In summary, as a consequence of weight loss and/ or deterioration of brain tissue, dilatation of the ventricular system is an important change that occurs with brain aging. The most studied structures are the third ventricle, due to its relationship with thalamic atrophy, and the lateral ventricles due to their association with the periventricular white matter and the basal nuclei.

In this sense, some authors consider that the ventricles grow at an average rate of 2.9%/year, after 70 years, this may be almost double that of young adult individuals²⁴⁻²⁷. In contrast, other authors indicate that this rate seems to decrease in healthy older individuals^{28,29}.

Conclusions

The present study provides a method for morphometric quantification of the lateral ventricles and a normative database, confirming that the volume of the lateral ventricles shows a significant effect as a function of age associated with aging. The implemented neuroimaging protocol allows obtaining global brain volume parameters, with an effective measurement precision level, which guarantees its introduction in the clinical environment. In correspondence with its statistical behavior, it can be used as a standardized morphometric pattern in a population with normal neurocognitive functions and promises to become a sensitive diagnostic tool for the individual diagnostic classification of cerebral atrophy. Additional research is required to validate its potential clinical utility.

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Conflicts of interest

All authors declare that they have no conflicts of interest with this research or with the publication of its results.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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