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Contribución original

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Fractal characterization of normal cerebral ventricles in t2-wheigthed magnetic resonance imaging

Caracterización fractal de ventrículos cerebrales normales en imágenes de resonancia magnética ponderadas en T2

Abstract

Introduction: The fractal geometry describes adequately the irregularity of the natural objects such as the cerebral ventricles, which are irregular structures that can be characterized through the Box-Counting method.

Objective: This research aims to develop a new methodology of geometric characterization of the cerebral ventricles, based on the fractal geometry for the analysis of normal cerebral ventricles.

Methods: Based on the Box-Counting method, the fractal dimensions of the both lateral ventricles of a normal adult were obtained. Sequential cephalic-caudal 4mm axial slices were acquired on T2-WI, and the differences and similarities of the lateral ventricles were established using the Ventricular Intrinsic Mathematical Harmony.

Results: The fractal dimension of the left lateral ventricle had values between 1.0641 and 1,3599, and in the right lateral ventricle had values between 0.8931 and 1.3219.

Conclusion: A new morphometric measure of the cerebral ventricles was developed based on the fractal geometry for its use as an objective and reproducible measure.

Keywords

brain, cerebral ventricle, fractal, fractal geometry, lateral ventricles.

Resumen

Introducción: Las dimensiones fractales permiten caracterizar matemáticamente la irregularidad de las formas naturales como los son las estructuras cerebrales. Los ventrículos cerebrales son objetos irregulares que pueden ser estudiados mediante esta geometría.

Objetivo: La investigación pretende desarrollar una caracterización en el espacio fractal de Box-Counting del ventrículo cerebral normal del adulto.

Métodos: Con fundamento en el método Box-Counting, se analizó la estructura geométrica de las imágenes obtenidas mediante TAC de un sujeto normal. Para ello se tomaron las imágenes de cortes cada 4mm y se midieron las dimensiones fractales de los ventrículos cerebrales, determinando además la Armonía Matemática Intrínseca Ventricular entre las imágenes consecutivas de cada ventrículo.

Resultados: Las dimensiones fractales presentaron valores entre 0.8931 y 1.3599, con valores de AMIV entre 0 y 2, mostrando la capacidad de la metodología de caracterizar la estructura irregular de los ventrículos cerebrales.

Conclusiones: Los resultados constituyen una nueva medida morfométrica para los ventrículos cerebrales, que permitió establecer medidas características de normalidad de utilidad como referencia para determinar la presencia de alteraciones ventriculares.

Palabras clave

cerebro, ventrículo cerebral, fractal, geometría fractal, ventrículos laterales.

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Introduction

Due to an impossibility to perform trustable Euclidian measures that could be associated to structures with complex and irregular shapes in different scales,[1,2] Benoit Mandelbrot in 1975 developed the fractal geometry, geometry that allows characterization of the irregular objects. This advance allowed him to work in a measure of the irregularity of objects, denominated as fractal dimension (FD). For non-mathematical fractals, characterized by superposition between its parts, considered as wild fractals, the FD is calculated with the Box-Counting method.[3,4]

There are different examples of application of fractal geometry in medicine, including laboratory and clinical sets: evaluation of diagnosis, follow-ups and results of any therapeutic intervention.[5–9]

Even though, in many cases, determining the FD by itself is not enough to establish differences for clinical practice, making it necessary to establish mathematical concepts for its evaluation. For example, like it was in an experimental model of coronary re-stenosis, where the morphometric of histology was evaluated, based on the processing of the FDs of the arterial layers, using the term of Arterial Intrinsic Mathematical Harmony (AIMH),[10] that can differentiate healthy versus sick arteries, with an accuracy of 10^30. This made place to a generalization of all possible fractal arterial structures, from the normal lumen to the total occlusion of the arterial lumen.[11] In other clinical project, the fractal dimension of the branching of the left coronary artery from diastole to systole in angiography was evaluated, differentiating patients with and without severe arterial occlusive disease.[12] Likewise, different diagnoses of the left cardiac ventricle in ventriculogram[13] and echocardiography[14] have been established, relating its FDs. Different authors have also shown its clinical applications in erythrocytary diagnosis[15], cervical uterine paraneoplastic lesions[16], and cardiac hemodynamics.[17] Fractal geometry has been applied to the measurement of cerebral structures, analysis of electroencephalograms, and functional Magnetic Resonance Imaging (MRI) as well.[18,19] Thus, demonstrating that the fractal geometry is a complementary important tool able to characterize states of normality and disease.[20,21]

The cerebral ventricles are evaluated with MRI for clinical practice through the use of lines for determining lengths and using Euclidian formulas for establishing volumes or approximated areas. Clinical MRI is based on the electromagnetic activity of spins of active atomic nuclei of hydrogen (protons and neutrons). Voxel-based MRI, by the way could be very accurate for establishing measures, based on three-dimensional occupation of matter.[22]

However, these measurements do not take into account completely the irregularity of cerebral structures, thus some important information can be ignored that could be determinant for clinical decisions and are based on statistic probabilistic significance. There is no other published work regarding the fractal characterization of the cerebral ventricles. This paper aims to develop a new objective and reproducible histological morphometric measurement for the characterization of the cerebral ventricles with the application of the fractal geometry.

Methods and Materials

Definitions

Fractal: Irregular object, from the Latin "fractus": irregular, fractioned.

Fractal dimension: A not-dimensional numeric measurement that determines the degree of the irregularity of a fractal.

For this work, it was used the definition for FD of

$$D = \frac{LogN(2^{-(K+1)}) - LogN(2^{-K})}{Log\,2^{k+1} - Log\,2^{k}} = Log_2 \frac{N(2^{-(k+1)})}{N(2^{-k})}$$

Box-Counting:
Where N (2^{-k}) is a function of the grade of partition of the k grid, and corresponds to the number of squares occupied by the object in the grid with partition 2^{-k}.

Procedure

Sequential cephalic-caudal 4mm axial slices of a T2-WI sequence of a non-contrast MRI of the head were acquired from a healthy patient with a General Electric SIGNA HD.XT. 1.5 Tesla. All images were processed in software developed by previous researches for the calculation of FDs with the Box Counting method.[12,11] The borders of the both lateral ventricles were delineated. Posteriorly, the number of squares occupied by the ventricles in the different slices was established. Based on these values the FD of the Box-Counting was obtained for each ventricle in the different slices using the equation D (see definitions). Finally, the Ventricular Intrinsic Mathematical Harmony (VIMH) was calculated, mathematically defined as the degree of similarity or difference between two FDs when comparing the two units and its significant digits. Two FDs present a VIMH of 0 if they have differences between the units. For example with 0,786 and 1,234: there is a VIMH of 1 if they have an equal value between the units but differentiate between each other in the first significant digit, as it is with 1,242 and 1,433; therefore, an IVMH of 2 will correspond to equal values to the unit and the first significant digit, as it is the case of 1,563 and 1,543, and then in the same way sequentially.

Bioethical considerations

This work meets the standards of medical ethics committees of the sponsoring institution of research and with the Helsinki Declaration of 1975, updated in 2000. It complies with the scientific, technical and administrative standards for health research, based on the resolution No. 008430 of 1993, and specifically title 11 concerning research on human beings, to be classified in the category of research without risk, as mathematical calculations on results of tests are done made a voluntary without coercion, not affecting the patient and respect their integrity and anonymity.[23]

Results

It was found that the cerebral lateral ventricles were observed in 4 out of 8 the adapted MRI slices. (Figure 1) For the both lateral ventricles of each 4 images the FD was obtained. The FD presented variations between 0,8931 and 1,3598. For the right lateral ventricles FDs ranged between 0,8931 and 1,3219 (Table 1), while the values of the degree of irregularity of the left ventricles were between 1.0641 and 1.3598. The degree of similarity between the parts of the ventricles were obtained when finding the VIMH for each ventricle in the different slices, as each image is a section of a three dimensional object. The values of the VIMH (Table 2) were higher for the lateral left ventricle on two of the three comparisons, showing that there is a greater degree of similarity between the parties to the left ventricle compared with the right. Additionally, the comparison of the images of the right ventricle of the slices 7 and 8 showed a greater self-organization than those of the left ventricle of the same slice, but in the other two comparisons the left ventricles had greater VIHM values.

Figure 1. Images adapted to process of Box-Counting. a. Limits of the ventricles are outlined. b. Superposition de la rejilla de 20 pixels.

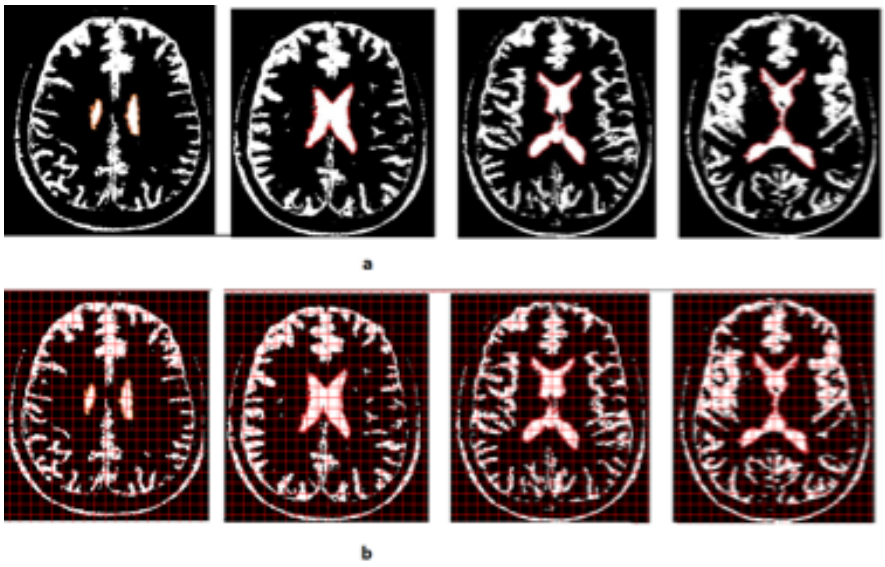

Figure 2. Image adapted to process of Box-Counting. a. This is an example of the measurements; both lateral ventricles are outlined (corresponding to the slice 5). b. Superposition of a 20-pixel Grillage.

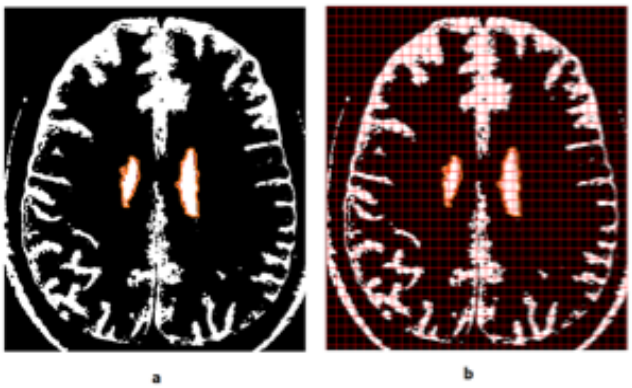

Table 1. The fractal dimensions of the right al lateral ventricles for each of the studied slices.

Image (#)	Left DF	Right DF
5	1,0780	1,3219
6	1,0641	0,8931
7	1,3599	1,1793
8	1,2283	1,1829

FD = Fractal Dimension.

Table 2. Ventricular Intrinsic Mathematical Harmony values for comparisons between the images.

VIHM between the images #	Left	Right
5 and 6	2	0
6 and 7	1	0
7 and 8	1	2

VIMH= Ventricular Intrinsic Mathematical Harmony.

Discussion

This is the first work were the Box-Counting method was applied for quantification of the degree of irregularity of the cerebral ventricles. This can be useful as a new reference for future studies of measuring of ventricles in patients with different diseases. Therewith, a new measurement for evaluation of the self-organization between the measures of the same ventricle in different slices was performed. This can also be a reference of normality in the future, for detecting the presence of ventricular alterations. However, this measure should be performed in larger series of healthy individuals to increase accuracy.

The measures conventionally used in a clinical fashion, especially in the Emergency Room, are based on Euclidean measurements and on the use of formulas to make approximations regarding the volume or size of specific structures. Even though, because of the irregularity of the structures, there is potentially important clinical information that can be lost by using Euclidean geometry on irregular objects. Additionally, the objectivity and the reproducibility of the measurements are difficult, which may involve variations in inter- and intra-observer interpretation.

In contrast, the measurements obtained by fractal geometry are an objective and reproducible method suited to the characteristics of brain structures, which provides clinical information that can be useful not only to assess the initial state of a patient but also for the purpose of monitoring their changes over time.

Fractal geometry has been successfully used for the objective characterization of different cellular and histological structures in medicine. For example, Hayano *et al*.[6, 24] performed fractal measures over Computed Tomography Angiography images of the liver, and made direct correlations with the degree of heterogeneity of tumors, for the evaluation of anti-angiogenic treatment, and for the survival of patients with hepatocellular carcinoma. In the same way, Fiz *et al*.[7] used fractal measures of ultrasound images of pulmonary nodules, differentiating benign and malignant nodules. Meanwhile, Talu performed fractal measures that could differentiate the microvasculature of the retina of patients with diabetic macular edema, which allowed making an earlier diagnosis of the disease.[9] Other comparisons between fractal dimensions of parts of a structure, or the whole structure, or its dynamics have been studied in other experimental and clinical phenomena.[10, 12-14,25]

In the brain, the fractal characterization was performed with MRI, obtaining important information regarding normal changes that occur during aging.[26] Reishofer *et al*.[27] also observed differences between FDs of cerebral structures in MRI of healthy patients and patients with arteriovenous malformations, giving information of the clinical behavior of these lesions. Besides, Wang *et al*. made fractal analysis of electroencephalograms of ictal and inter-ictal states, achieving a characterization of each one, with a high sensibility (>90%), demonstrating that it can be used in the automatic identification of seizures.[28]

In this paper, we present a fractal characterization of cerebral lateral ventricles. Furthermore, the concept of VIMH is implemented, whereby variations of fractal auto-organization of the cerebral ventricles can be observed in different slices. In further studies there should be an implementation of this methodological analysis of different neurological diseases and cerebral lesions demonstrating changes in geometry of cerebral structures, in order to develop diagnostic and therapeutic clinical applications.

This work is based on a form of physical-mathematical non-causal thinking, which seeks to establish the underlying laws of the different phenomena within the cerebral ventricles. This research perspective has established diagnoses and predictions in areas such as immunology,[29] molecular biology,[30] infectology,[31,32] neonatal and adult cardiology,[33,34] and predicting epidemics,[35] obtaining results of clinical, experimental and public health utility. Further studies are needed to implement the fractal characterization of the cerebral ventricles and VIMH in the clinical context of patients with diseases of the central nervous system.

Conclusions

This research is based on physical and mathematical theories that provides a new tool for clinical practice for a future adequate evaluation of the irregularity of the cerebral ventricles using the Box-Counting method and the VIMH.

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Conflict of interest

The authors declare no conflict of interest.

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Bibliography

1. Mandelbrot B. *¿Cuánto Mide la Costa de Gran Bretaña? Los Objetos Fractales*. Barcelona: Tusquets Editores; 1987. 27–50.
2. Mandelbrot B. *The Fractal Geometry of Nature*. Barcelona: Tusquets Editores; 2000.
3. Peitgen H-O, Jürgens H, Saupe D. Limits And Self Similarity. *Chaos and Fractals.* New York: Springer-Verlag; 1992. 135–82.
4. Peitgen H, Jürgens H, Saupe D. Length, Area and Dimension: Measuring Complexity and Scaling Properties. In: Peitgen H, Jürgens H, Saupe D, eds. *Chaos and Fractals.* New York: Springer-Verlag; 1992. 183–228.
5. Al-Kadi OS. A multiresolution clinical decision support system based on fractal model design for classification of histological brain tumours. *Comput Med Imaging Graph.* 2015;41:67-79.
6. Hayano K, Yoshida H, Zhu AX, Sahani D V. Fractal analysis of contrast-enhanced CT images to predict survival of patients with hepatocellular carcinoma treated with sunitinib. *Dig Dis Sci.* 2014;59(8):1996–2003.
7. Fiz JA, Monte-Moreno E, Andreo F, *et al*. Fractal dimension analysis of malignant and benign endobronchial ultrasound nodes. *BMC Med Imaging.* 2014;14:22.
8. Metze K. Fractal dimension of chromatin: potential molecular diagnostic applications for cancer prognosis. *Expert Rev Mol Diagn.* 2013;13(7):719-735.
9. T?lu S. Multifractal geometry in analysis and processing of digital retinal photographs for early diagnosis of human diabetic macular edema. *Curr Eye Res.* 2013;38(7):781–792.
10. Rodriguez J, Mariño M, Avilan N, *et al*. Medidas fractales de arterias coronarias en un modelo experimental de reestenosis. Armonía matemática intrínseca de la estructura arterial. *Rev Colomb Cardiol.* 2002;10:65–72.
11. Rodríguez J, Prieto S, Correa C, *et al*. Theoretical generalization of normal and sick coronary arteries with fractal dimensions and the arterial intrinsic mathematical harmony. *BMC Med Phys.* 2010;10(1):1–6.
12. Rodríguez J, Prieto S, Correa C, *et al*. Fractal diagnosis of severe cardiac dysfunction Fractal dynamic of the left coronary branching. *Rev Colomb Cardiol.* 2012;19(5):225–32.
13. Rodríguez J, Prieto S, Correa C, *et al*. Fractal diagnosis of left heart ventriculograms Fractal geometry of ventriculogram during cardiac dynamics. *Rev Colomb Cardiol.* 2011;19(1):18–24.
14. Rodríguez J, Prieto S, Ortiz L, *et al*. Mathematical diagnosis of pediatric echocardiograms with fractal dimension measures evaluated through intrinsic mathematical harmony. *Rev Colomb Cardiol.* 2010;17(2):79–86.
15. Correa C, Rodríguez J, Prieto S, *et al*. Geometric diagnosis of erythrocyte morphophysiology. *Int J Med Med Sci.* 2012;3(11):715–720.
16. Prieto S, Rodríguez J, Correa C, *et al*. Diagnosis of cervical cells based on fractal and Euclidian geometrical measurements: Intrinsic Geometric Cellular Organization. *BMC Med Phys.* 2014;14(1):2.
17. Rodríguez J, Correa C, Melo M, *et al*. Chaotic cardiac law : Developing predictions of clinical application. *Int J Med Med Sci.* 2013;4(2):79–84.
18. Spasic S, Culic M, Grbic G, *et al*. Spectral and fractal analysis of cerebellar activity after single and repeated brain injury. *Bull Math Biol.* 2008;70(4):1235–1249.
19. Lahmiri S, Boukadoum M. Alzheimer's disease detection in brain magnetic resonance images using multiscale fractal analysis. *ISRN Radiol.* 2013;2013:627303.
20. Di Ieva A, Grizzi F, Jelinek H, *et al*. Fractals in the Neurosciences, Part I: General Principles and Basic Neurosciences. *Neuroscientist.* 2013;20(4):403–417.
21. Di Ieva A, Esteban FJ, Grizzi F, *et al*. Fractals in the Neurosciences, Part II: Clinical Applications and Future Perspectives. *Neuroscientist.* 2015;21(1):30–43.
22. Bitar R, Leung G, Perng R, *et al*. MR Pulse Sequences : What Every Radiologist Wants to Know but Is Afraid to Ask. *Radio Graphics.* 2006;26(2):513–538.
23. Ministerio de Salud de Colombia. Resolución número 8430 DE 1993. 1–19.
24. Hayano K, Lee SH, Yoshida H, *et al*. Fractal analysis of CT perfusion images for evaluation of antiangiogenic treatment and survival in hepatocellular carcinoma. *Acad Radiol.* 2014;21(5):654–660.
25. Rodríguez J. New diagnosis aid method with fractal geometry for pre-neoplasic cervical epithelial cells. *Rev UDCA Actual y Divulg Científica.* 2011;1(14):15–22.

26. Liu JZ, Zhang LD, Yue GH. Fractal dimension in human cerebellum measured by magnetic resonance imaging. *Biophys J.* 2003;85(6):4041–4016.
27. Reishofer G, Koschutnig K, Enzinger C, *et al*. Fractal dimension and vessel complexity in patients with cerebral arteriovenous malformations. *PLoS One.* 2012;7(7):e4114–4118.
28. Wang Y, Zhou W, Yuan Q, *et al*. Comparison of ictal and interictal EEG signals using fractal features. *Int J Neural Syst.* 2013;23(6):1350028.
29. Rodríguez J, Bernal P, Álvarez L, *et al*. Plasmodium falciparum MSP-1 and EBA-140 peptides prediction of binding to HLA class II probability, combinatory and entropy applied to peptide sequences. *Inmunología.* 2010;29(3):91–9.
30. Rodríguez J, Bernal P, Prieto S, *et al*. Theory of malaria peptides with high-affinity binding to red blood cells. Theoretical predictions of new binding peptides and predictive mutations of critical amino acids. *Inmunología.* 2010;29(1):7–19.
31. Rodríguez J, Prieto S, Correa C, *et al*. Predictions of CD4 lymphocytes' count in HIV patients from complete blood count. *BMC Med Phys.* 2013;13(1):3.
32. Rodríguez J, Prieto S, Correa C, *et al*. Teoría de conjuntos aplicada al recuento de linfocitos y leucocitos: predicción de linfocitos T CD4 de pacientes con virus de la inmunodeficiencia humana/sida. *Inmunología.* 2013;32(2):50–56.
33. Rodríguez J, Prieto S, Domínguez D, *et al*. Mathematical-physical prediction of cardiac dynamics using the proportional entropy of dynamic systems. *Int J Med Med Sci.* 2013;4(9):370–381.
34. Rodríguez J, Prieto S, Flórez M, *et al*. Physical-mathematical diagnosis of cardiac dynamic on neonatal sepsis : predictions of clinical application. *Int J Med Med Sci.* 2014;5(5):102–108.
35. Rodríguez J. A method for forecasting the seasonal dynamic of malaria in the municipalities of Colombia. *Rev Panam Salud Pública.* 2010;27(3):211–218.

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