ORIGINAL ARTICLE

COMPARATIVE ANALYSIS OF FRACTAL DIMENSIONS OF HUMAN CEREBELLUM: IMPACT OF IMAGE PREPROCESSING AND FRACTAL ANALYSIS METHODS

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ABSTRACT

The aim: To compare the values of the fractal dimensions of human cerebellum obtained using different algorithms of image preprocessing and different methods of fractal analysis.
Materials and methods: The study involved 120 people without structural changes in the brain (age 18-86 years, 55 men and 65 women). T1- and T2-weighted MR brain images were studied. Fractal analysis was performed using box counting and pixel dilatation methods. Fractal dimensions of cerebellar tissue as a whole, cerebellar cortex and its individual layers, cerebellar white matter were measured and compared to each other and to fractal dimension of cerebellar white matter determined in cadaveric cerebella.
Results: It was no significant difference between fractal dimension values of cerebellar tissue as a whole measured on T1 and T2 weighted magnetic resonance images of cerebellum, and fractal dimension values measured on the same images using different methods of fractal analysis – pixel dilatation and box counting. T2 weighted images are preferable for fractal analysis of different components of cerebellar tissue. Segmentation according to pixel luminance is the preferable image preprocessing method for fractal analysis of cerebellar cortex as a whole, individual cortical layers and cerebellar tissue as a whole; skeletonizing of cerebellar magnetic resonance images is the preferable method of the image preprocessing for fractal analysis of cerebellar white matter.
Conclusions: The algorithm of image preprocessing, magnetic resonance imaging sequence and method of fractal analysis should be chosen according to aim of quantitative study of cerebellar magnetic resonance images and features of the studied structure of cerebellum.

KEY WORDS: cerebellum, fractal analysis, fractal dimension, magnetic resonance imaging, neuroimaging

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INTRODUCTION

In recent years, fractal analysis is increasingly used in morphological investigations of fractal biological structures. Fractal analysis provides quantitative and objective determination of the spatial complexity degree of different structures of human organism [1-3].

Spatial configuration of different structures of human cerebellum has fractal properties. Cerebellar white matter has a sophisticated tree-like branching pattern. It may be considered as fractal structure as well as cerebellar cortex, which forms a three-dimensional convoluted foliated structure, duplicating external contour of white matter [4]. Fractal analysis is one of the main morphometric techniques that may provide a quantitative morphological assessment of cerebellum [5-9].

For fractal analysis it is necessary to clearly define the boundaries of the studied structure. In view of this, the true fractal dimension of some cerebellar structures can be determined only via study of the anatomical sections of cerebellum, because neuroimaging methods may not have sufficient resolution to clearly define the boundaries of cerebellum and the boundaries between different components of cerebellar tissue. In our previous study, we determined the fractal dimension of white matter on the midsagittal sections of cadaveric cerebella [10]. In further studies we determined the fractal dimensions of cerebellum and its individual components (white matter and cortex) on the magnetic resonance (MR) images [11-13]; but we faced the problem of adapting these results to clinical practice to quantify MR brain images.

Different image preprocessing algorithms and various fractal analysis methods were used in different studies. The box counting method was applied in the studies of Akar E. at al. [5-7] and in the study of Wu Y.T. et al. [8]; the pixel dilatation modification was applied in the study of Liu J.Z. at al. [9]. In our previous studies we applied both methods: box counting [10, 11] and pixel dilatation [12, 13].

Therefore, to determine the best algorithm for fractal analysis of cerebellar MR images, we decided to compare the true FD values measured in cadaveric cerebella [10] and FD values measured in T1- and T2-weighted MR brain images, with different image preprocessing algorithms and using different fractal analysis methods [11-13]. The present study is a continuation and summarizing of our previous research on fractal analysis of human cerebellum [10-13].

THE AIM

The aim of the study was to compare the values of human cerebellum fractal dimensions obtained using different

algorithms of image preprocessing and different methods of fractal analysis.

MATERIALS AND METHODS

The study involved 120 people without structural changes in the brain (age 18-86 years, 55 men and 65 women). All participants provided written informed consent.

The conclusion of the Commission on Ethics and Bioethics of Kharkiv National Medical University confirms that the study was conducted in compliance with human rights, in accordance with current legislation in Ukraine, meets international ethical requirements and does not violate ethical standards in science and standards of biomedical research (minutes of the meeting of the Commission on Ethics and Bioethics of KhNMU №10 from 07.11.2018).

T1- and T2-weighted MR brain images were studied. MRI was performed on a 1.5 T MRI machine. The image parameters included the following. T1-weighted images: TE (echo time) was 14 ms, TR (repetition time) was 500 ms; section thickness was 5 mm; T2-weighted images: TE was 122 ms, TR was 4520 ms; section thickness was 5 mm. Sagittal MRI projection was chosen for the study (Fig. 1).

Initial preprocessing included segmentation of images. A 2 × 2-inch (128 × 128-pixels) fragments containing the midsagittal sections of the cerebella were copied from the digital magnetic resonance (MR) images (Fig. 1, A, D). The fragments of MR images were segmented using the Adobe Photoshop CS5 software. The structures surrounding the cerebella were initially removed from the images (Fig. 1, B, E), and the pixels in these areas were colored black (T1-weighted images, luminance value of 0 – Fig. 1, B) or white (T-2 weighted images, luminance value of 255 – Fig. 1, E). Segmentation was performed according to the pixels' luminance value using the "threshold" tool. The images were segmented into two components: the studied structure (colored white in T1-weighted images or colored black in T2-weighted images) and background (colored black in T1-weighted images or colored white in T2-weighted images). An empirical luminance threshold value of 100 was used for segmentation of T1- and T2-weighted MR images; it revealed the cerebellar tissue as a whole without segmentation into individual components (Fig. 1, C, F).

Fractal analysis was performed using two different methods: pixel dilatation method in the author's modification [14] and box counting method with the Image J software [15]; two-dimensional fractal dimensions (2D FD) were determined [11-13].

Initially, fractal analysis of cerebellar tissue as a whole was carried out using pixel dilatation method. Two fractal dimensions were measured: FD of T1-weighted images (FD(1)) and FD of T2-weighted images (FD(2)). T2-weighted images were more heterogeneous than T1-weighted images, thus, the T2-weighted images were chosen for the study of individual components of cerebellar tissue.

For the further investigations, we selected T2-weighted MR brain images of 30 young adults (18-30 years age range, 15 men and 15 women) among the MR images of 120 persons enrolled in the study. FD values were measured on the same MR images using two different methods of fractal analysis: pixel dilatation method (FD(3)) and box counting method (FD(4)).

Afterwards, the studied MR images were additionally segmented into individual components of cerebellar tissue (Fig. 2, A-E). For that purpose, the "threshold" tool was used. Fractal analysis of individual components of cerebellar tissue was carried out using the pixel dilatation method. We determined FD of cerebellar cortex as a whole (FD(5)), FD of granular layer of cerebellar cortex (FD(6)), FD of molecular layer of cerebellar cortex (FD(7)) and FD of cerebellar white matter (FD(8)).

After the initial segmentation, the image skeletonizing procedure was performed (Fig. 2, F). We used the "skeletonize" tool of Image J software. This tool revealed the main branches of the cerebellar white matter. FD of skeletonized images (FD(9)) was determined using a box counting method.

The obtained FD values were compared with each other and were compared to the FD values of cerebellar white matter obtained in our previous study of cadaveric cerebella [10] (FD(10), FD(11)). The study [10] was carried out on cadaveric specimens: 100 cerebella of people of both sexes who died from causes not related to brain diseases (62 male and 38 female; age range of 20-95 years). Cerebella were obtained during forensic autopsies. The macrophotographs of the midsagittal sections of cerebellar vermis were studied, the box counting method was utilized for fractal analysis; the counting was manual due to impossibility of the automatic image segmentation which is necessary for the automatic box counting with Image J software. The true values of FD of cerebellar white matter were determined (FD(10)). We additionally selected 14 cadaveric cerebella (20-30 years age range) for the present study and calculated FD value of the cerebellar white matter of those objects (FD(11)) to compare with FD values measured on 30 MR images of young persons (18-30 years age range).

A statistical data processing was performed using Excel 2010 software. The following values were calculated: the sample mean (M) and the standard error of the mean (m), the median value (Me, percentile 50) with interquartile ranges (the values of percentiles 25 and 75), the minimum (min) and the maximum (max) values. The significance of statistical differences between the FD values was assessed using the Kruskal-Wallis H test with Bonferroni adjustment for multiple comparisons. The significance level for all results was accepted as $p<0.05$.

RESULTS

We analyzed FD values of different structures of cerebellum, obtained using different image preprocessing algorithms and different methods of fractal analysis. The obtained values of the analyzed fractal dimensions of human cerebellum are listed in Table I and the distribution of the FD values is shown in Fig. 3. The statistical significance

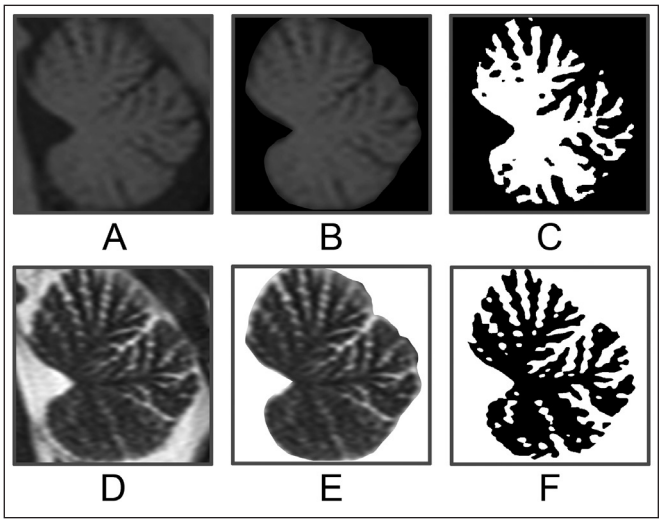

Fig. 1. Pre-processing of cerebellar MR images: segmentation of T1-weighted images (A, B, C) and T2-weighted images (D, E, F).

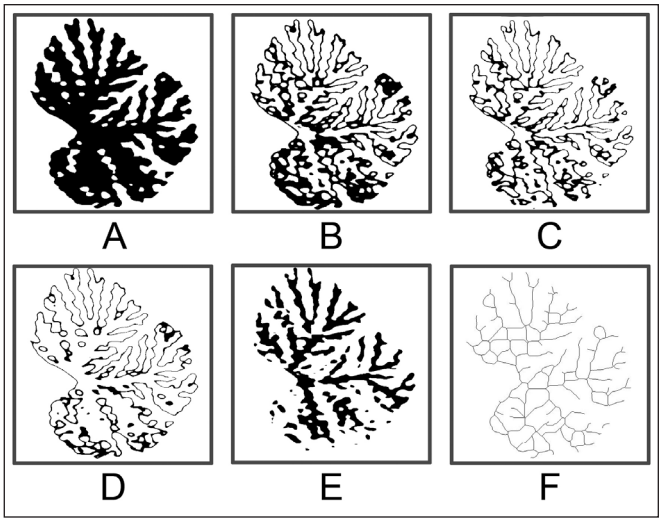

Fig. 2. Pre-processing of T2-weighted MR images of cerebellum. A-E – image segmentation using "threshold" tool: A – cerebellar tissue as a whole (threshold 100), B – cortex as a whole (difference between thresholds 100 and 80), C – granular layer of cerebellar cortex (difference between thresholds 90 and 80), D – molecular layer of cerebellar cortex (difference between thresholds 100 and 90), E – white matter (threshold 80). F – image skeletonizing using "skeletonize" tool: skeleton of white matter.

of the difference between FD values was assessed and null hypothesis was rejected; the difference between the mean ranks of compared FD values was statistically significant. Thus, the multiple paired comparisons between different FD values were provided.

It was no significant difference between FD values of cerebellar tissue as a whole, including FD(1) value measured on T1 weighted images using pixel dilatation method, FD(2) and FD(3) values measured on T2 weighted images using pixel dilatation method and FD(4) value measured on T2 weighted images using box counting method.

FD(1) and FD(2) values were measured on the MR images of the same persons, using the same image preprocessing and the same fractal analysis method (pixel dilatation), but *different MRI sequences* were utilized to obtain the studied MR images. The FD values determined on T1 and T2 weighted images were not significantly different and had close comparable parameters of statistical distribution. Therefore, T1 and T2-weighted MR images may be used for fractal analysis.

FD(3) and FD(4) values were measured on the T2-weighted MR images of the same persons and with the same image preprocessing, but *different fractal analysis methods* were applied. The FD values determined utilizing different methods of fractal analysis (FD(3) – pixel dilatation, FD(4) – box counting) coincided and were not significantly different. This indicates that both methods of fractal analysis may be used to determine FD values of cerebellar tissue as a whole.

All FD values of cerebellar tissue as a whole (FD(1-4)) were significantly different from the FD values of individual components of cerebellar tissue: FD(5-8), FD(9) (FD of skeletonized images) and FD of cerebellar white matter measured on cadaveric material (FD(10-11). There was significant difference between FD(5) value (cortex) and all other FD values, but there was no significant difference between values of FD(6) (molecular layer of cortex), FD(7) (granular layer of cortex) and FD(8) (white matter) compared to each other.

The FD values corresponding to cerebellar white matter were measured on the same T2-weighted MR images of the same persons, but with *different image preprocessing*: FD(8) – segmentation with a threshold of 80 and FD(9) – image skeletonizing. The FD(8) and FD(9) values were not significantly different.

The FD values were determined on the *different materials* (MR images and cadaveric material). FD values of cerebellar white matter measured on the MR images (FD(8) and FD(9)), were compared to FD values of white matter measured on the midsagittal sections of cadaveric cerebella. There was no significant difference between FD(8) and FD (10). But there was a significant difference between FD(9) and FD(10) ($p<0.05$). This may be caused by difference in the age range: 18-30 years for FD(9) and 20-95 years for FD(10). In our previous study, it was established that FD of cerebellar white matter had a significant strong negative correlation relationship with age ($r=-0.917$, $p<0.001$). According to this fact, we selected 14 cadaveric specimens (among 100) in the compatible age range (20-30 years) and calculated FD(11). There was no significant difference between FD(9) and FD(11). FD(9) and FD(11) values coincided and had close comparable parameters of statistical distribution and variance of the values. FD(8) values have a much larger variance compared to FD(9) and FD(11) values; this parameter may not be as accurate as the FD of skeletonized images (FD(9)). Thus, FD(9) (measured on skeletonized MR images) may be considered as a best parameter that corresponds to the true fractal dimension of the cerebellar white matter (FD(11)) which can be only measured by direct study of the anatomical sections of cadaveric cerebella. Skeletonizing of the cerebellar MR images is the preferred image pre-processing technique for fractal analysis of the cerebellar white matter.

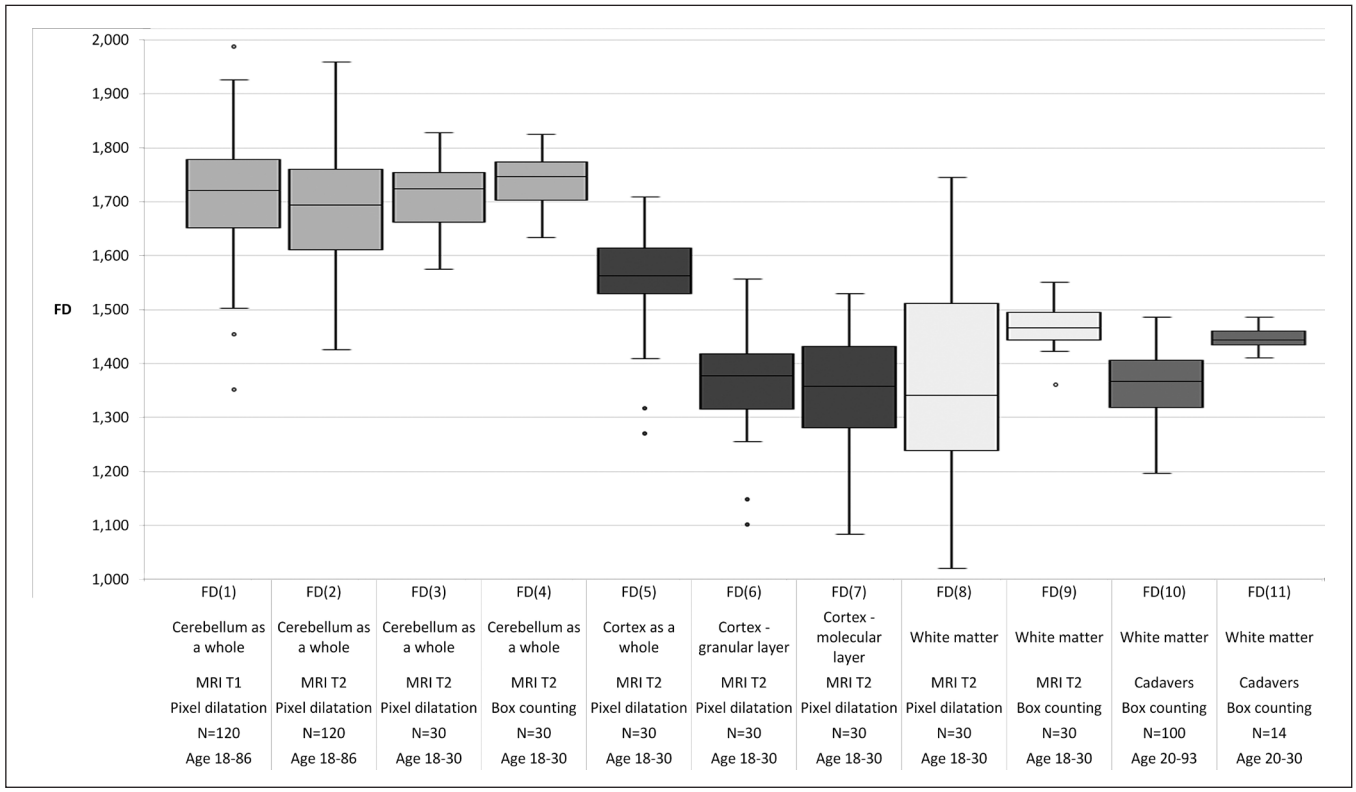

Fig. 3. The distribution of the fractal dimension values of human cerebellum.

Table I. The fractal dimension values of human cerebellum

FD	Cerebellar structure	Image type	Image preprocessing method	Pixels' luminance threshold	Fractal analysis method	Number of objects (N)	Age range, years	FD, M±m
FD(1)	Cerebellar tissue as a whole	MRI T1	segmentation	100	pixel dilatation	120	18-86	1.714±0.009
FD(2)		MRI T2						1.691±0.01
FD(3)						30	18-30	1.707±0.013
FD(4)					box counting			1.738±0.009
FD(5)	Cerebellar cortex as a whole	MRI T2	segmentation	100-80	pixel dilatation	30	18-30	1.564±0.018
FD(6)	Cerebellar cortex – granular layer			90-80				1.377±0.02
FD(7)	Cerebellar cortex – molecular layer			100-90				1.353±0.02
FD(8)	Cerebellar white matter	MRI T2	segmentation	80	pixel dilatation	30	18-30	1.318±0.05
FD(9)			skeletonizing		box counting 14			1.469±0.007
FD(10)		Macro-photo-graphs of cadaveric cerebella	visual assessment			100	20-95	1.372±0.006
FD(11)						20-30		1.447±0.005

DISCUSSION

Fractal analysis of MR brain images is an important area of modern neuroscience, since it allows diagnostics of various diseases of the nervous system. There are some studies which involved fractal analysis of human cerebellum [5-9]. The T1-weighted MR brain images were analyzed in all research works found in accessible literature. Different modifications of fractal analysis were applied: box counting [5-8] or pixel dilatation modification [9] and different fractal dimensions were determined: 2D (two-dimensional fractal dimension; the values vary from 1 to 2) [5, 6] or 3D (three-dimensional fractal dimension; the values vary from 2 to 3) [7-9]. Different components of cerebellar tissue were assessed (white matter and cortex), but FD of individual layers of cerebellar cortex were not measured in these studies.

In the studies of Akar E. at al. the 2D and 3D box counting methods were applied [5-7]. MR brain images were segmented into white matter, gray matter of cerebellum and cerebrospinal fluid. The mean value of 2D FD of cerebellar white matter was 1.49±0.06 and the mean value of the 2D FD of cerebellar gray matter was 1.56±0.05 [5, 6]. The mean value of 3D FD of cerebellar white matter was 2.26±0.05 and the mean value of the 3D FD of cerebellar gray matter was 2.49±0.04 [7].

In the study of Wu Y.T. et al. the 3D box counting method was utilized [8]. Automated 3D segmentation techniques were used; the cerebellar MR images were also segmented into white matter, gray matter and cerebrospinal fluid. The mean value of 3D FD of cerebellar white matter was 2.2746±0.0446 and the mean value of the 3D FD of cerebellar gray matter was 2.5267±0.0228 [8].

In the study of Liu J.Z. at al. the 3D pixel dilatation method was applied [9]. The image skeletonizing was used as a preprocessing method. The mean value of the 3D fractal dimension of the cerebellar white matter skeleton was 2.57±0.01 [9].

Thus, the present study and the studies of other researchers demonstrate that the values of the fractal dimension of cerebellum and individual components of cerebellar tissue may be quite different depending on utilized modification of the fractal analysis (box counting or pixel dilatation, two or three dimensional fractal analysis), type of studied material (MRI or cadaveric specimens), MR sequence (T1 or T2), and the algorithms of image preprocessing (segmentation, skeletonizing, etc.).

CONCLUSIONS

1. The values of fractal dimension of cerebellar tissue as a whole determined on the T1- and T2-weighted MR brain images were not significantly different; both MRI sequences may be used to obtain the MR scans for the fractal analysis.
2. There was no significant difference between FD values measured on the same images but using different fractal analysis methods – pixel dilatation and box counting; both methods give comparable results.
3. Segmentation of the T2-weighted MR brain images using "threshold" tool according to pixel luminance is the preferable image preprocessing method for fractal analysis of cerebellar cortex as a whole, individual cortical layers and cerebellar tissue as a whole.
4. Skeletonizing of the MR images is the preferable image preprocessing method for fractal analysis of cerebellar white matter.
5. The algorithm of image preprocessing, MRI sequence and method of fractal analysis should be chosen according to the aim of study and features of the studied structure.

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