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Fractal dimension analysis of cerebellum in Chiari Malformation type I

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ABSTRACT

Chiari Malformation type I (CM-I) is a serious neurological disorder that is characterized by hindbrain herniation. Our aim was to evaluate the usefulness of fractal analysis in CM-I patients. To examine the morphological complexity features of this disorder, fractal dimension (FD) of cerebellar regions were estimated from magnetic resonance images (MRI) of 17 patients with CM-I and 16 healthy control subjects in this study. The areas of white matter (WM), gray matter (GM) and cerebrospinal fluid (CSF) were calculated and the corresponding FD values were computed using a 2D box-counting method in both groups.

The results indicated that CM-I patients had significantly higher ($p < 0.05$) FD values of GM, WM and CSF tissues compared to control group. According to the results of correlation analysis between FD values and the corresponding area values, FD and area values of GM tissues in the patients group were found to be correlated. The results of the present study suggest that FD values of cerebellar regions may be a discriminative feature and a useful marker for investigation of abnormalities in the cerebellum of CM-I patients. Further studies to explore the changes in cerebellar regions with the help of 3D FD analysis and volumetric calculations should be performed as a future work.

1. Introduction

As a serious pathological condition described by Professor Hans Chiari in 1891 [1], Chiari Malformation type I (CM-I) is characterized by the downward displacement of cerebellar tonsils, which are rounded structures located at the bottom of each cerebellar hemisphere, into the spinal canal [2,3]. Radiologically, descent of the cerebellar tonsils more than 5 mm into the cervical canal through the foramen magnum leads to the diagnosis of CM-I [4]. Although the brainstem and the fourth ventricle may be smaller or slightly deformed, they are in their normal position. Most CM-I patients involve syringomyelia, which is an abnormal dilatation of spinal canal creating a small cavity that can involve a collection of cerebrospinal fluid (CSF) [5]. CM-I may arise from several reasons, including altered CSF circulation dynamics that disrupt the equilibrium of intracranial pressure [2], incomplete development of occipital bones and small posterior cranial fossa (PCF) that results in an overcrowding of cerebellum [6–8].

Patients with CM-I may show several symptoms with various degrees of severity. The most frequent symptom is the headache in the back of the head. Another common condition is the pain in neck and shoulders [9,10]. A list of secondary signs include dysarthria, a condition that affects speech quality of a person [11]; balance and gait problems [12]; nystagmus, a condition involving repetitive, involuntary eye movements that cause limited vision [13]; and sleep apnea [14]. An important consideration of this anomaly is that a wide variety of its signs and symptoms may result in misdiagnoses with some other neurological diseases including, migraine and multiple sclerosis (MS) [6] due to an absence of a particular diagnostic test that associates the symptoms of CM-I with its anatomical conditions [11].

Midline sagittal T1 weighted magnetic resonance imaging (MRI) provides the best viewpoint for displaying herniation [15]. Computed tomography and neurological tests are additional diagnostic methods that may be used for the identification of CM-I [16]. Another common examination method is the use of a phase-contrast (PC) cine MRI that allows the assessment of CSF flow and velocity [6,17,18]. Treatment of CM-I is achieved by a surgical operation called posterior fossa decompression [19]. Strong debate on the pathophysiology of this syndrome creates a disagreement on particular aspects of surgical process [11]. Restoration of CSF flow is the primary goal of the surgeons who consider CSF flow blockage to

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be the actual cause of CM-I symptoms [20,21]. On the other hand, if surgeons believe that the small size of the posterior fossa is the major reason for CM-I symptomatology, their surgical approach will intend to enlarge the PCF region.

Many studies have been performed so far to investigate the neurological characteristics of CM-I syndrome. The Majority of these previous studies were related to assessment of the morphological properties of the cerebellum and nearby regions, such as the brainstem and fourth ventricle. Sagittal MRI slices of brain were generally used to measure the morphological characteristics of the PCF. These measurements can be classified into linear and volumetric measurements. Linear measurements involve the length of tonsillar descent, which can be calculated by taking the distance between the cerebellar tips and a line drawn from the basion to the opisthion, and the length of the clivus and supraocciput. On the other hand, total volumes of the posterior fossa, CSF and brain are other type of measurements for the volumetric evaluation of CM-I [6–8,22–24]. Furthermore, there are additional studies investigating CSF flow and velocity in order to figure out the effects of CSF flow patterns on the severity of CM-I symptoms [20,21,25]. Great deal of observations and efforts have been performed until now to enlighten this anomaly; nevertheless, the exact mechanisms of CM-I pathophysiology are still unclear. Therefore, new features have to be found and new methods have to be employed in order to get a more clear understanding of this anomaly.

The fractal geometry introduced by Mandelbrot in 1982 [26] is a concept to describe continuous spatial or temporal phenomena that are not differentiable. Fractal objects having fractal properties that contain self-similarity, numerous quantity of details and scale invariance may be found anywhere in nature, such as plants, trees, snowflakes and coastlines. The FD analysis approaches may be employed to describe and classify the structural details in complex objects by producing a single numeric value. This value, as a quantitative measure of morphological complexity, has been used to examine a wide range of objects in biology and medicine [27–29]. Additionally, FD analysis has been proposed as a new method and widely used in the field of neuroscience to measure object complexity and to examine structural variations in some conditions and disorders, such as gender differences [30], identification of early stage atherosclerosis [31], epilepsy [32], schizophrenia [33,34], age-related micro-structural white matter (WM) changes [35], detection of tumors [36,37], multiple sclerosis [38], Alzheimer's disease [39], stroke [40], and cerebellar degeneration [41]. Besides, dynamic changes of neural system morphology during brain growth or degeneration can be quantified by employing fractal analysis [42–44]. Furthermore, it has been demonstrated that fractal approaches are suitable for studying shape complexity of cerebral structures including WM, gray matter (GM), and WM tracts [38,41,44]. The purpose of the present study is to compute the FD value of cerebellar WM, GM and CSF tissues for an investigation of structural differences between patients with CM-I and healthy controls.

Segmentation of brain MRI is an important step in the analysis of brain images for the purpose of understanding the influence of several conditions such as neurodegeneration, epilepsy and trauma on brain structures. Different methods have been proposed to automatically segment the brain MR images into different clusters of tissues. These methods can be classified into several categories such as classification-based segmentation, contour-based segmentation, region-based segmentation and knowledge-based segmentation [45]. A simple technique is the use of thresholding algorithm which splits an image into different classes using threshold intensity values [46]. Besides that, other classification-based methods include statistical classification based approaches such as Markov random field [47], expectation maximization [48] and clustering based methods like fuzzy-c means [49]. Additionally, edge based methods and active contours approach [50] can be regarded as the examples of contour-based segmentation methods. Moreover, region-based techniques involve methods based on watershed [51], region growing and split-and-merge [52] algorithms. On the other hand, there are a number of software packages, which automatically perform a set of image processing routines such as bias field correction, skull splitting and automated segmentation. Statistical Parametric Mapping (SPM), FMRIB's Software Library (FSL) are some of these packages and they have been widely used in neuroimaging studies [38,40,41,57,61].

We hypothesized that the altered physical conditions of CM-I, such as tonsillar descent and overcrowding of cerebellum, may lead to the variations in morphological complexities of cerebellar tissues such as GM, WM and CSF. Since FD value is a convenient numeric descriptor for morphological complexity of structural details in brain tissues and it has been widely used in differential diagnostic studies, we have chosen this method to investigate structural complexity variations of cerebellum between healthy controls and patients with CM-I. To the best knowledge of the authors, this is one of the first studies that uses FD analysis to evaluate structural cerebellar complexity in CM-I patients. The aim of the present study is to make an effort to contribute the redefinition of the anomaly, which is still in progress, and assist the diagnosis, treatment and management of patients with this syndrome.

2. Materials and methods

2.1. Patients and MR acquisition

Data used in this study were obtained from MRI records of the department of Radiology, Mehmet Akif Ersoy Cardio-Thoracic Surgery Training and Research Hospital and Medicana International Hospital, İstanbul, from 2013 to 2014. Brain images of 16 healthy subjects (8 males and 8 females, 16–50 years age range) and 17 CM-I patients (7 males and 10 females, 16–55 years age range) were used in this study (Table 1). No statistically significant differences were found in gender and groups as a result of a chi-square analysis ($p=0.732$). Brain MRI of subjects, who were diagnosed as CM-I anomaly by an experienced radiologist and by a neurosurgeon, were included in the patient group in this study. On the other hand, having any neurological and psychiatric conditions other than CM-I was accepted as exclusion criteria for MRI data of patients. The experimental procedures of the study were approved by the Ethical Committee of Fatih University.

Three-dimensional T1-weighted human MR brain images were acquired from a Siemens Symphony Magnetom Aera 1.5 T MR scanner (Erlangen, Germany). The image parameters include: 24

Table 1
Demographical and Clinical data of subjects (mean ± std.dev.).

	Patients	Controls	*p*-Value
Age	37.94 ± 10.57	37.56 ± 9.21	0.914
Gender (M/F)	7/10	8/8	–
GM area	897.8 ± 134.92	649.79 ± 65.61	< 0.001*
WM area	394.16 ± 125.55	487.82 ± 79.37	0.016*
CSF area	405.51 ± 102.01	393.25 ± 55.05	0.673
GM FD	1.68 ± 0.07	1.56 ± 0.05	< 0.001*
WM FD	1.57 ± 0.07	1.49 ± 0.06	0.001*
CSF FD	1.37 ± 0.13	1.16 ± 0.06	< 0.001*

M/F: male/female, GM area: area of cerebellar gray matter (mm^2), WM area: area of cerebellar white matter (mm^2), CSF area: area of cerebrospinal fluid (mm^2), GM FD: gray matter fractal dimension, WM FD: white matter fractal dimension, CSF FD, cerebrospinal fluid fractal dimension.

* Less than the significance *p*-Value of 0.05.