Analysis of sub-cerebellar regions in patients with Chiari Malformations

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ABSTRACT
Chiari Malformations are serious neurological defects involving herniation of hindbrain tissues such as cerebellar tonsils, brainstem and IV ventricle into the spinal canal through the foramen magnum. By the severity of cerebellar descent, these malformations are classified into four different types. Clinically the least obvious and the mildest one is named as type I and defined as the descent of cerebellar tonsils into the cervical canal more than 5 mm. Magnetic Resonance Images (MRI) of brain in the sagittal plane provides the best clues in the diagnosis of the Chiari Malformation type I (CM-I). Previous studies investigated the morphological characteristics of cerebellum and nearby regions such as brain stem and fourth ventricle. Aim of this study is to analyze the cerebellar regions in chiari patients and healthy controls to search for the discriminative properties between the two groups. Sagittal brain MRI of eleven chiari patients and gender matched controls were used in order to examine the area of sub-cerebellar tissues such as gray matter (GM) and white matter (WM) and the area ratio between GM and WM. A graphical user interface (GUI) for implementing image processing techniques was developed using MATLAB environment. By means of GUI, the region embracing the whole cerebellum tissue on the mid-sagittal MR images were manually extracted. In addition, using Statistical Parametric Mapping (SPM) package the MRI slices were segmented into GM and WM tissues. Using the extracted cerebellum region as a mask, the cerebellar GM and WM tissues were achieved and the corresponding areas were computed by counting the number of pixels on each GM and WM slice. According to the statistical results, it has been found that cerebellar GM areas of the patients are significantly higher than the values of controls. As a consequence, this approach may provide a discriminative feature between patients with CM-I and health control subjects.

Keywords: Chiari malformation, magnetic resonance imaging, segmentation, gray matter, white matter

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INTRODUCTION
Chiari Malformations are a group of developmental anomalies that involve the herniation of cerebellar tonsils, brainstem and IV ventricle into the spinal canal through the foramen magnum [1]. The mildest of these anomalies is designated as Chiari Malformation type I (CM-I) and radiologically defined as the downward displacement of the cerebellar tonsils below the foramen magnum more than 5 mm [2]. Chiari Patients may show several symptoms of different severity ranges. The most frequent one is the headache in the back of the head. Another common condition is the pain in neck and shoulders [3]. Additionally, a number of secondary symptoms have been reported such as ataxia which is the presence of abnormal, uncoordinated movements, dysarthria which is a motor speech system problem, balance problems, dizziness and muscle weakness [4]. Midline sagittal MR images provide a proper view for the diagnosis of the anomaly. In addition, a cine phase-contrast MRI may also be used for the cerebrospinal fluid (CSF) flow assessment for diagnostic purposes [5]. Surgical procedure used for the treatment of Chiari is posterior fossa decompression. The aim of this operation is to create more space around the herniation and bring back natural circulation of CSF [6].

Several studies have been made to investigate the neurological conditions of CM-I. In these studies, linear and volumetric measurements were carried out using the MRI slices and computer tomography (CT) scans of brain for the evaluation of morphological characteristics of posterior cranial fossa (PCF) [5,7-9]. As a linear criterion, the length of the tonsillar descent was measured as an indicator of the Chiari severity. Moreover, the volume of PCF, CSF and the whole brain were calculated for the volumetric evaluation of CM-I [5, 8]. Additional studies were also carried out for the
assessment of the CSF flow and velocity in order to understand the effects of CSF flow dynamics on the symptoms intensity of the Chiari anomaly [10, 11]. Previous studies investigating the PCF features [5,7-9] and CSF flow dynamics [10,11] have provided valuable information related to CM-I; nevertheless, there are still unclear points regarding the pathophysiology and symptomatology of this anomaly. Therefore, the aim of this study is to search for some elucidatory and discriminative features in order to contribute the ongoing redefinition of Chiari anomaly. In the present study, the areas of cerebellar substructures such as white matter (WM) and gray matter (GM) were calculated and the ratio between these area values were found in order to investigate the morphological variations between the Chiari patients and healthy controls.

PATIENTS AND METHODS

Subjects and MRI Acquisition

Brain images of 11 healthy subjects (5 males and 6 females, 16 - 50 years age range) and 11 Chiari I patients (4 males and 7 females, 16 - 55 years age range) were used in this study (Table 1). The experimental procedures of the present study were approved by the Ethical Committee of Fatih University. The image data were obtained from the MRI records of Department of Radiology, Mehmet Akif Ersoy Cardio-Thoracic Surgery Training and Research Hospital and Medicana International Hospital, Istanbul. T1-weighted human brain MRI were acquired from a Siemens Symphony Magnetom Aera 1.5 T MR scanner (Erlangen, Germany). Image parameters: sagittal slices of 5mm, echo time 9.8 ms, repetition time 511 ms, flip angle 90º, FOV 23 cm, and matrix size 512x512.

Image Processing

The image processing procedures which consist of four steps were carried out using the midline sagittal MRI slices. For the facilitation of these procedures, a graphical user interface (GUI) was built using the MATLAB 8.2® user interface development environment. The initial step of image processing is filtering of MRI images based on 2D median filtering using a 3x3 kernel in order to improve the signal to noise ratio. Secondly, the region that contained the entire cerebellum was manually extracted from the midline sagittal brain images in order to use as a mask for obtaining cerebellar GM and WM (Figure 1a and 1b). In the third place, the sagittal MRI slices were registered to SPM8 utility and the WM and GM images were produced as a result of this application. After that, using the MATLAB based GUI, the masking operations were performed to get the images that contained solely the cerebellar GM and WM tissues (Figure 1c and 1d). In the final step, the areas of GM and WM regions were calculated by counting the nonzero pixels in these regions and by multiplying the result with the distance of each pixel in mm in both vertical and horizontal dimensions.

Statistical Analysis

SPSS® (version 20.0) statistical software package were used to evaluate the results statistically. The independent sample Student’s t-test was used to compare the results of area analysis between the patients and controls. Levene’s test was used to test the homogeneity of groups’ variances.

![Figure 1. Manual Extraction and GM and WM segmentation processes. A - determination of cerebellum borders, B - extracted cerebellar region, C - segmented gray matter tissue, D - segmented white matter tissue.](image-url)
The results of this study showed that the GM area of cerebellum in patients with Chiari was significantly higher (p<0.001) than the corresponding area values of healthy controls as shown in Figure 2.

We could not find a significant difference in cerebellar white matter area between Chiari patients and healthy controls (p=0.261) which is shown in Figure 3. Finally, our results demonstrated that the ratios between the cerebellar GM and WM were significantly higher (p=0.041) in patients than the ones in controls. The box-plot diagram in Figure 4 displays this condition.

**CONCLUSION**

CM-I is a neurological disorder of hindbrain tissues which is characterized by the descent of cerebellar tonsils more than 5 mm into the cervical canal through the foramen magnum. It has been reported that patients with chiari have smaller volumes of PCF and CSF compared to the healthy controls [5]. Additionally, some studies indicated that patients with chiari have altered dynamics of CSF flow and velocity [10, 11]. According to the results of some previous studies, the exact mechanism of the pathophysiology of Chiari is not well understood which leads to the difficulties in treatment and management of patients [10, 12]. Therefore, the purpose of the present study is to find new informative characteristics by performing an area analysis on cerebellar structures including GM and WM. The results indicated that Chiari patients have larger GM area values compared to controls. Similarly the ratio between the GM and WM area values are lower in controls. Thus, our findings suggest that altered physical conditions in CM-I may result in changes in cerebellar GM and WM. To confirm our results, further studies should be performed with a larger number of participants and based on new analysis techniques.

**DECLARATION OF INTEREST**

The authors declare no conflict of interest for this study.
REFERENCES


