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Volumetric Analysis of the Cerebellum with the volBrain Method in Patients with Migraine

Migrenli Hastalarda volBrain Yöntemi ile Serebellumun Hacimsel Analizi

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ABSTRACT

Migraine is a recurrent headache syndrome with a wide spectrum of symptoms. The diagnosis of migraine is mostly made retrospectively, taking into account the characteristics of the headache and other symptoms. It is not known enough how migraine headache starts and in which brain regions it occurs. It is known that changes in the excitability of brainstem nuclei affect endogenous pain mechanisms and unilateral involvement of trigeminovascular structures are effective mechanisms in migraine development. Understanding the role of the cerebellum in migraine disease is a fairly new topic in neuroscience. 19 Mıgraıne Patıents (MP) and 14 Healthy Controllers (HC) partıcıpated ın our study. For the volumetric analysis of the cerebellum, the ceres method of volbrain, which is an automatic brain volume calculation method, was used and the volumes of the cerebellum structures were obtained. SPSS 22.0 program was used for the analysis of the data and the level of significance was accepted as $p<0.05$. There is a significant increase in gray matter volumes of MP crus I, Crus II, lobus VIIB VIIIA, VIIIB and IX. When the cerebellum structures were examined according to the disease duration and attack frequency, a significant increase was found in the gray matter volumes of the cerebellum, crusII, lobule VIIB, and lobule VIIIA. These regions showed a positive correlation with attack frequency. As a result, posterior cerebellar structures show an activity that overlaps with the frequency of attacks and the duration of the disease. Volumetric or functional changes in the cerebellum indicate that it is effective in the pathophysiology of migraine pain.

Keywords: Cerebellum, Migrain, volBrain

ÖZ

Migren, geniş bir semptom yelpazesine sahip tekrarlayan bir baş ağrısı sendromudur. Migren tanısı çoğunlukla baş ağrısının özellikleri ve diğer semptomlar dikkate alınarak geriye dönük olarak konur. Migren baş ağrısının nasıl başladığı ve hangi beyin bölgelerinde meydana geldiği yeterince bilinmemektedir. Beyin sapı çekirdeklerinin uyarılabilirliğindeki değişikliklerin endojen ağrı mekanizmalarını etkilediği ve trigeminovasküler yapıların tek taraflı tutulumunun migren gelişiminde etkili mekanizmalar olduğu bilinmektedir. Migren hastalığında serebellumun rolünü anlamak, sinirbilimde oldukça yeni bir konudur. Çalışmamıza 19 Migren Hastası (MH) ve 14 Sağlıklı Kontrolör (SK) katıldı. Serebellumun hacimsel analizi için otomatik beyin hacmi hesaplama yöntemi olan volbrain ceres yöntemi kullanılmış ve beyincik yapılarının hacimleri elde edilmiştir. Verilerin analizinde SPSS 22.0 programı kullanılmış ve anlamlılık düzeyi $p<0.05$ olarak kabul edilmiştir. MH crus I, Crus II, lobus VIIB VIIIA, VIIIB ve IX'un gri madde hacimlerinde önemli bir artış var. Hastalık süresi ve atak sıklığına göre serebellum yapıları incelendiğinde serebellum, crusII, lobül VIIB ve lobül VIIIA'nın gri cevher hacimlerinde anlamlı artış saptandı. Bu bölgeler, saldırı frekansı ile pozitif bir korelasyon gösterdi. Sonuç olarak posterior serebellar yapılar, atakların sıklığı ve hastalığın süresi ile örtüşen bir aktivite göstermektedir. Beyincikte hacimsel veya fonksiyonel değişiklikler migren ağrısının patofizyolojisinde etkili olduğunu gösterir..

Anahtar Kelimeler: Migren, Serebellum, volBrain

Ethics committee approval of the study was received from Karadeniz Technical University Faculty of Medicine Scientific Research Ethics Committee (24.02.2023/134). *This study is presented as an oral presentation in Abstracts of the 10th Anatomy Winter Days.*

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INTRODUCTION

Migraine is a recurrent headache syndrome with a wide spectrum of symptoms [1, 2]. Before diagnosing migraine to the patient, it is very important to take a detailed anamnesis. The diagnosis of migraine is mostly made retrospectively, taking into account the characteristics of the headache and other symptoms. Usually, medical and neurologic examinations are normal. magnetic resonance imaging (MRI) and Computed tomography in patients suffering from headaches exclude other causes of pain [3]. However, these anomalies are often benign. Laboratory tests and imaging methods are often used to exclude other secondary causes of headache. Laboratory findings and physical and neurological examination results are usually normal and are mostly used to exclude secondary headache causes. [4, 5]. Patients often complain of a typical change in mood or behavior that occurs suddenly and may show psychological, neurological, constitutional or autonomic characteristics [6]

It is not known enough how migraine headache starts and in which brain regions it occurs [7]. It is known that changes in the excitability of brainstem nuclei affect endogenous pain mechanisms and unilateral involvement of trigeminovascular structures are effective mechanisms in migraine development. Understanding the role of the cerebellum in migraine disease is a fairly new topic in neuroscience. Recent studies suggest that the cerebellum plays a role in pain perception [8, 9]. Since approximately 2/3 of migraine patients are motion sensitive and 1/4 may have paroxysmal vertigo, the detection of vestibular abnormalities in migraine patients suggests that there may be a relationship with the vestibulocerebellar system [1, 10]. Cerebellar activity in response to trigeminal nociceptive input in migraine patients has been demonstrated in numerous functional imaging studies in migraine patients. Studies with neuroimaging methods have shown that the brain volumes and activities of patients with migraine are different compared to healthy controls [11]. However, it is not clearly understood whether such changes reflect the current status of frequent attacks and the longitudinal consequences of migraine attacks.

Our aim in this study. To compare the cerebellum volumes of healthy controls with migraine patients, to contribute to the pathophysiology of the disease by determining the changes in the cerebellum caused by the frequency of attacks and the duration of the disease.

METHOD

In our study, MRI of 20 migraine patients (MP), aged 18-50 years, who were diagnosed with migraine without any pathological lesions, and 20 healthy controls (HC), who applied to the Neurology Outpatient Clinic of Karadeniz Technical University, were analyzed. As a result of the analysis, those with SNR values greater than 20 were included in the study [12]. The MRI of the groups included in the study (19 MP and 14 HC) were checked by the radiologist to see if there was a pathological lesion and no pathology was found.

Magnetic resonance imaging and volume analysis

3T Siemens magnetome magnetıc resonance (MR) device was used in all MRI scans.

MR protocol;

High resolution T1 weighted mprage sequence:
Sagittal, Repetition Time(tr):1900 ms,
Echo Time(te):2.67 ms,
Fov:250 mm,
Matrix:256x256
Slice Thickness: 1 mm

The ceres method of volbrain, which is an automatic brain volume calculation method, was used for the volumetric analysis of the cerebellum. The Volbrain method is an online automated segmentation method where researchers can analyze MR images without the need for any infrastructure. First of all, to obtain the volumes of the cerebellar lobules;T1 images were converted to niftii format and the vhttps://volbrain.upv.es/index.php page has been accessed. Files converted to niftii format by clicking on Ceres 1.0 segment were submitted. The process took approximately 10 minutes and at the end of the process, the result report was downloaded to the computer and the total and gray matter volumes of the cerebellar lobules were obtained in cm3 [12-14].

Statistical analysis

The conformity of the data to normal distribution was evaluated with Q-Q charts and Shapiro-wilk test.. An independent two-sample t-test was used for quantitative variables in comparisons between groups. SPSS 22.0 program was used for the analysis of the data and the level of significance was accepted as $p<0.05$.

Ethical statement

This study was carried out using MR images obtained with the approval of the scientific research ethics committee of the Karadeniz Technical University Faculty of Medicine. Participants were asked to sign an informed consent form before the MRI scan.

RESULTS AND DISCUSSION

The mean age of migraine patients (MP) and healthy controls (HC) included in our study was MP 38±6 and HC 34±8. When the cerebellar lobule volumes of the MP and HC are examined, there is a significant increase in the gray matter volumes of the MP's crus I, Crus II, lobus VIIB, VIIIA, VIIIB and IX (Figure 1).We grouped the patient group as those who had a maximum of 9 attacks per month and those who had 10 or more attacks per month. There was a substantial increase in gray matter volumes of the cerebellum, crusII, lobule VIIB, lobule VIIIA (total, right, left) of those with attacks of 10 or more (Figure2).

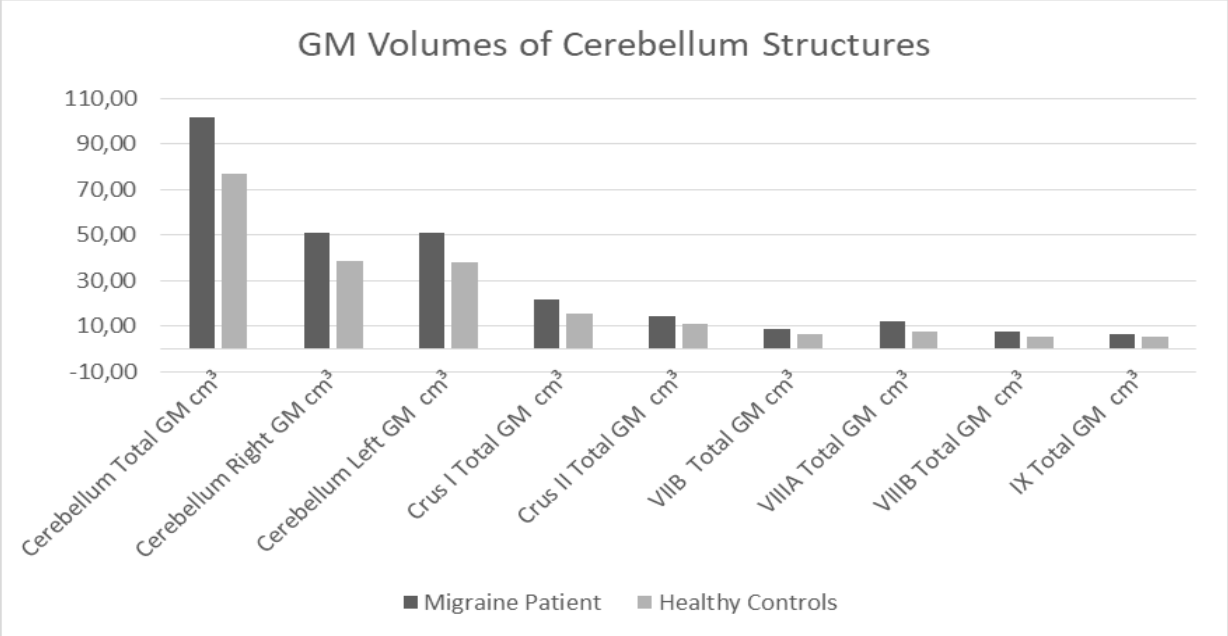

Figure 1. GM Volume Values Of Cerebellum Structures Of MP and HC Groups ($p<0.05$)

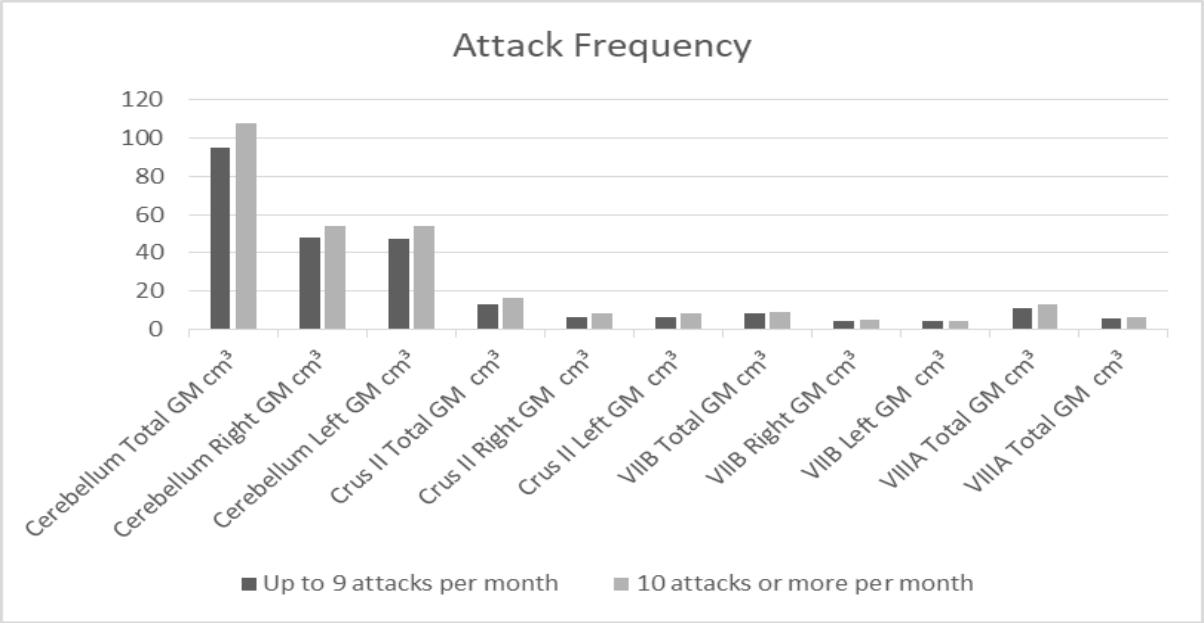

Figure 2. The Effect of Attack Frequency in the MD and SC Groups on The Cerebellum (p<0.05)

There is an increase in gray matter volumes of cerebellum, crusII, lobule VIIB (total, right, left) and lobule VIIIA (total, right) in patients who have been sick for more than 5 years compared to those who have been sick for less than 5 years (Figure 3). Attack frequency was positively correlated in cerebellum total, crus II, lobule VIIB and lobule VIIIA (Figure 4).

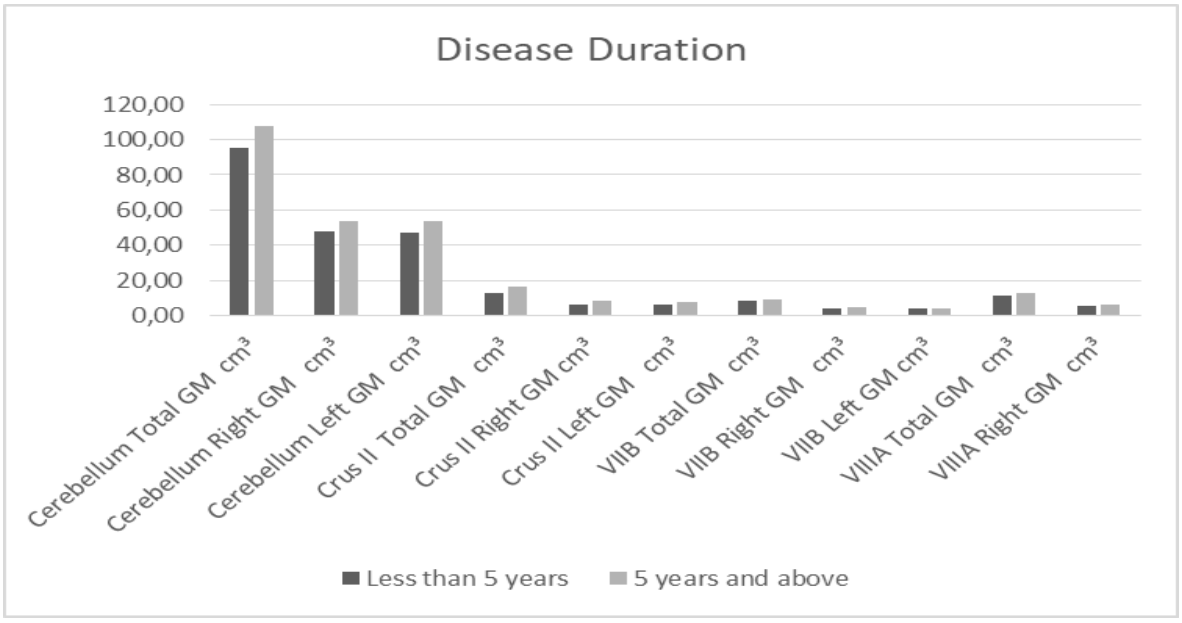

Figure 3. Relationship Between Gray Matter Volumes of Cerebellum Structures and Disease Duration (p<0.05)

In studies, brain and cerebellum volumes of healthy controls and migraine patients were examined and structural differences were found in posterior cerebellum gray matter volumes. However, these structural differences vary [15, 16]. In our study, an

increase was found in the gray matter volumes of the posterior cerebellum, including crus I, crus II, lobule VII, and VIII, compared to healthy controls. There are few studies that specifically examine the cerebellum structures in migraine patients. Jan Mehnert et al., in their study, found an increase in volume in the cerebellum crus I, crus II lobules VIIA and VIIIB lobules. This situation is similar to our study [2]. Crus I and Crus II prefrontal cortex and posterior lobules are functionally closely associated with posterior parietal cortical area. Crus II region is activated during mental tasks and is associated with frontal lobe afferents [8, 17]

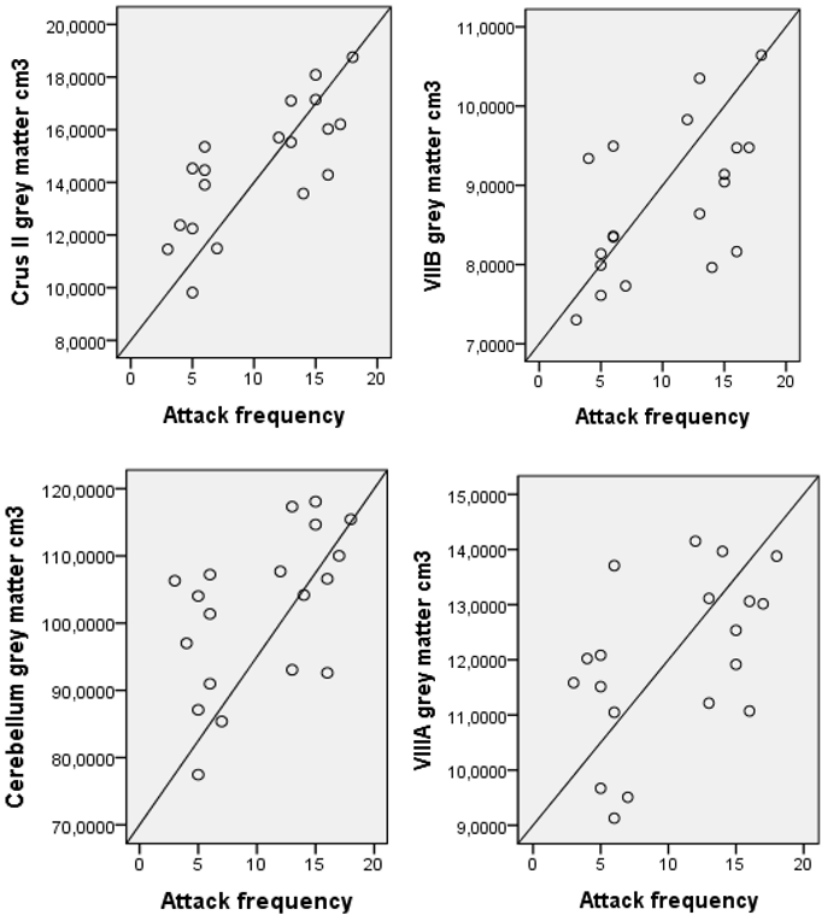

Figure 4. Correlation Graph of Attack Frequency, Total Cerebellum, Crus II, Lobule VIIB and VIIIA GM Volumes (p<0.05)

The findings of our study suggest that crus 1 and crus 2 and their cerebral connections may have a role in pain perception and cognitive processing in migraine patients.

In recent studies, it is said that the cerebellum is related to emotion, cognition and learning as well as motor and coordination functions. However, the role of the cerebellum in pain is not fully known. [9].

Studies have shown that the gray matter volumes of the cerebellum vary with the duration of the disease and the frequency of attacks [18, 19].

Our findings support these studies. However, these changes are thought to be due to the difference in the methods used and the number of participants. The fact that disease duration and attack frequency are correlated with gray matter volume is significant in terms of establishing a causal relationship between cerebellum and migraine.

In our study, there was an increase in the frequency of attacks and an increase in the volume of the cerebellum (total, right, left), crus II, lobule VIIB (total, right, left) VIIIA, (total) gray matter during the long disease. Although the mechanism of the cerebellum

in headache prognosis is unclear, there is evidence that large cerebellum volume is associated with diffuse body pain. In functional MR studies, it is stated that the posterior lobes of the cerebellum are activated in anticipation of pain and there is a difference in cortical excitability in headache frequency [18]. Fear arising from the expectation of pain may be a prognostic factor for chronic pain. Although there are balance changes and symptoms of vertigo in migraine, there are few studies that specifically evaluated cerebellar function between attacks or during attacks [19, 20].

CONCLUSION AND RECOMMENDATIONS

As a result, posterior cerebellar structures show an activity that overlaps with the duration of the diseaseand the frequency of attacks. Volumetric or functional changes in the cerebellum indicate that it is effective in the pathophysiology of migraine pain.

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