Volume Calculation of Brain Structures in Migraine Disease by Using MriStudio

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ABSTRACT

Migraine is a neurological disorder that is known as headache and accompanies attacks of neurological and gastrointestinal symptoms and prevents daily life activities of the person. In the literature, the volume changes of many structures in the brain have been investigated using brain magnetic resonance images (MRI) of migraine patients, but it has not yet been investigated whether there is a comprehensive and detailed volume change involving all the structures of the brain. The purpose of this study is to examine the brain structures in a wide range and to determine in which regions the volume changes. In this study, 25 healthy subjects and 25 migraine patients were included in the study. SPSS 15.0 program was used for statistical analysis. The Mristudio was used in our study when we examined the volumes of migraine patients and brain structures of healthy individuals. Statistically significant volume changes were found in the volumes of structures found in the brain frontal, parietal, occipital, temporal lobes. Volumetric changes were assessed in terms of duration of illness and frequency of attacks. In conclusion, our study is compatible with migraine pathophysiology. Structural changes in the brain are thought to be a risk factor for migraine. The evidence on the relationship of regional gray matter volumetric change detected in migraine is unclear. We believe that this ambiguity is caused by the method used.

Key Words: Brain Volume, Migraine, MRIStudio, Attack Fever, Disease Duration

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Introduction

Migraine is a common disease in the community. For more than 80% of migraine patients starting age is 30 and earlier. For sociodemographic variables, given the prevalence of migraines varies according to age and sex. Migraine attacks have caused serious loss of work force (Seneviratne *et al.,* 2013).

It is possible to put a positive diagnosis of migraine (Evans RW). Physical and neurological examination, laboratory examination results usually normal and more are used to rule out causes of secondary headache. (Stephen D Silberstain & 2002). Magnetic Resonance Imaging (MRI) is the most popular method among the routine radiological examinations, where the most studies and researches are done all over the world, the rapid development is obtained (Bushong, 1980). Also, with MRI, images can be obtained from multiple planes without changing the patient's position (Viola *et al.*, 2004). Many imaging studies have shown that migraine patients cause many changes in the brain of attacks (Seneviratne *et al.*, 2013).

These changes include increased cortical excitability, increased gray matter volume in some fields of the brain, decreased in some areas, increased brain blood flow, changes in the pain modulation system (Bartolini *et al.*, 2004; May 2009; Welch *et al.*, 2001).

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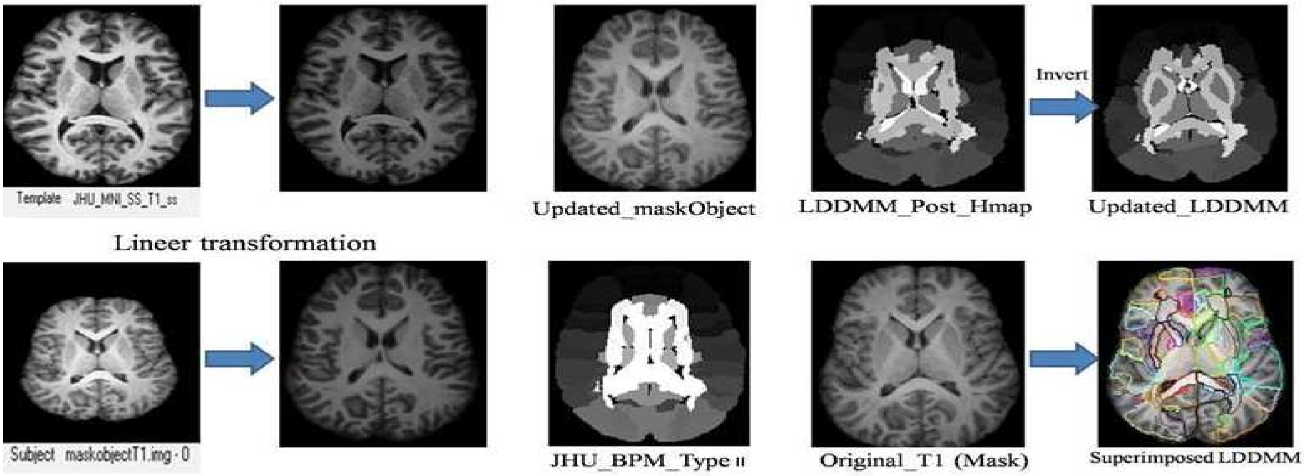

Figure 1. A schematic diagram of the image normalization process

Many studies have investigated the effects of on brain volume changes or cognition(Acer *et al.*, 2007). There are many different segmentation methods in which manual and automated techniques are used in assessing brain volume(Sahin *et al.*, 2007). Brain damage seen in migraineurs is associated with migraine attack frequency and duration of illness, and this damage is foreseen to appear after about fifteen years from the onset of the illness(Schmitz *et al.*, 2008). Magnetic Resonance (MR) has become a preferred method for macroneuroanatomic studies because of its excellent quality and contrast (Looi *et al.*, 2008).

Methods

In our study, brain MR images taken from the department of radiology of the patients who were diagnosed with migraine in the neurology department of Karadeniz Technical University Faculty of Medicine and taken as DICOM file were used. The study included 25 patients with migraine ages ranging between 18 and 70 and any neurological, psychiatric and cognitive disorders has not yet been included 25 healthy subjects of the same age range. Average volume values are expressed in mm^3. Before starting to work, approval of ethical committee of scientific researches of Black Sea Technical University Faculty of Medicine.

Statistical Analysis

SPSS 15.0 program was used for statistical analysis. The obtained values were presented as mean ± standard deviation. A nonparametric test and the Mann-Whitney U test was used in comparison between the patient and healthy subjects. $p < 0.05$ was considered significant.

MR Protocol

Images were obtained using the Siemens 1.5 Tesla MR in the Black Sea Technical University Radiology Department. High resolution T1 weighted MPRAGE sequence: sagittal, repetition time (tr): 1900 msec, echo time (te): 2.67 ms, fov: 250 mm, matrix: 256x256 slice thickness 1 mm. We used Mristudio in our image processing program. Masked images of each participant were first linearly transformed using Affine AIR transformation with trinear interpolation and then matched using LDDMM inverse LDDMM and then inverse ROI using reverse AIR were applied to the ROI atlas. ROI within the original brain area were obtained. For each participant, volume values (mm^3) were obtained for 186 parcelated brain structures (Figüre I)(Acer *et al.*, 2018; Faria *et al.*, 2011; Faria *et al.*, 2010; Izbudak *et al.*, 2015). The generated ROI were examined visually for control purposes.

Results

When we examined the mean age of migraine patients (MP) and healthy individuals (HI) participating in our study, the mean age of MP was 37 ± 9 and the mean age of HI was 35 ± 7. When we examined the volumes of some structures in the subcortical region, it was found that migraine patients had significant volume increase in left and right thalamus volumes compared to HI ($p<0.05$) (mm^3). (Table 1).

When we examined the frontal, parietal, temporal, and occipital regions of the brain, significant volume differences between MP and HI were detected (p<0.05)(mm³), (Table 2).

When we look at the changes in the duration of the disease over some brain regions, we found significant reductions in the volume of the central nervous system in some cases over a period of 5 years compared to those with a disease duration of less than 5 years (p<0.05) (mm³), (Table 3).

When the frequency of migraine episodes on the brain and central nervous system is examined, volumetric reductions in the brain and central nervous system have been found to be associated with more than 10 episodes per month compared to less than 10 episodes per month (p<0.05) (mm³), (Table 4).

Table 1. Volumetric results of some structures in the subcortical region

Subcortical Areas	MP		HI		p
	Mean	Standard Deviation	Mean	Standard Deviation	
Thalamus left	5546	570	4972	758	0.01*
Thalamus right	5413	443	5022	786	0.04*
Putamen left	3623	283	3508	453	0.29
Putamen right	3945	515	4013	1465	0.83
Globus Pallidus left	1291	153	1362	231	0.21
Globus Pallidus right	1582	775	1566	576	0.93

**p<0.05 mean volume values are expressed in mm³.*

Table 2. Volumetric results of some structures in frontal, parietal, temporal and occipital regions

	MP		HI		p
	Mean	Standard Deviation	Mean	Standard Deviation	
Postcentral Gyrus Left	10855	2227	10227	1340	0.23
Postcentral Gyrus Right	10919	1678	11427	1372	0.24
Precentral Gyrus Left	12576	3360	11865	1581	0.34
Precentral Gyrus Right	15103	2802	14694	1438	0.52
Superior Parietal Gyrus Left	8163	1347	8057	896	0.75
Superior Parietal Gyrus Right	6473	1059	6111	940	0.21
Supramarginal Gyrus Left	9550	1452	8603	1281	0.02*
Supramarginal Gyrus Right	9837	2789	8847	1572	0.13
Angular Gyrus Left	7437	965	7018	761	0.09
Angularis Gyrus Right	12335	1690	11330	1469	0.03*
Superior Frontal Gyrus Left	24187	2485	22188	2987	0.01*
Superior Frontal Gyrus Right	22359	2910	20356	2337	0.01*
Mıddle Frontal Gyrus Left	23368	2963	22273	2862	0.19
Mıddle Frontal Gyrus Right	23993	5174	21920	2740	0.08
Inferior Frontal Gyrus Left	10877	2655	9775	1044	0.06
Inferior Frontal Gyrus Right	9324	1806	8469	1221	0.06
Superior Temporal Gyrus Left	18627	3628	17648	2107	0.42
Superior Temporal Gyrus Right	18150	3899	17242	2275	0.73
Mıddle Temporal Gyrus Left	20029	4005	17336	2330	0.006*
Mıddle Temporal Gyrus Right	17964	5081	15651	2979	0.003*
Inferior Temporal Gyrus Left	12646	4795	11206	1959	0.184
Inferior Temporal Gyrus Right	13270	5974	12370	1789	0.961
Superior Occipital Gyrus Left	3026	438	2866	535	0.42
Süperior Occipital Gyrus Right	2495	781	2553	574	0.92
Mıddle Occipital Gyrus Left	16127	2982	15262	2936	0.33
Mıddle Occipital Gyrus Right	16877	3923	15339	2756	0.10
Inferior Occipital Gyrus Left	3981	722	3799	567	0.25
Inferior Occipital Gyrus Right	5391	1059	4878	676	0.03*

**p<0.05 mean volume values are expressed in mm³.*

Table 3. Effect of disease duration on some brain structures

Some brain zone volumes	Disease duration				p
	1 to 4 years		5 years and over		
	Mean	Standard Deviation	Mean	Standard Deviation	
Superior Frontal Gyrus Left	25653	1927	23362	2425	0.02*
Inferior Frontal Gyrus Left	12377	3830	10033	1162	0.03*
Precentral Gyrus Right	16601	3799	14260	1662	0.04*
Nucleus Cerebral Left	11508	2154	10208	804	0.04*

**p<0.05 mean volume values are expressed in mm³*

Table 4. Impact of attack frequency on some brain structures

Some Brain Zone Volumes	Attack Frequency				p
	Up to 9 Attacks per Month		10 or more attacks per month		
	Mean	Standard Deviation	Mean	Standard Deviation	
Thalamus Right	5563	246	5145	591	0.02*
Superior Parietal Gyrus Left	8672	1062	7258	1374	0.01*
Globus Pallidus Left	1348	121	1191	157	0.01*

**p<0.05 mean volume values are expressed in mm³*

Discussion and Conclusion

The automatic segmentation method used in our work has higher accuracy than the manual technique. The accuracy of the automatic segmentation method was supported by other studies (Acer *et al*., 2007; Sahin *et al*., 2007)

Migraine patients whose disease duration was more than 5 years had a decrease in gray matter volumes compared to patients who were less than 5 years. The 5-year disease duration is thought to be sufficient for brain volume changes to occur. Nociceptive signals / information in the meninges are transmitted to the second row of trigeminovascular neurons in the spinal trigeminal nucleus, from which they are transmitted to the parabrachial area, hypothalamus, lateral preoptic area, zona incerta and thalamustine nuclei (Noseda & Burstein 2013). The significant volume differences in thalamus in our study suggest that our study is compatible with migraine pathophysiology and that this area plays an important role in migraine. More clear results can be obtained if these areas in the Diencephalon region can be measured individually.

Yılmaz *et al*., measured voxel-based morphometry (VBM) volumetric brain measurements in 23 patients with migraine without aura and 24 non-migraine headaches, but did not find any significant difference in brain volume and cerebellum volume between the two groups. In the same study, there was no significant relationship between cerebellar volume and duration of illness and attack frequency (Yilmaz-Kusbeci *et al*., 2010).

Maleki *et al*., in patients with frequent and frequent episodes of migraine with functional migraine, measurements of functional MRI showed increased left thalamus, pons, left hypothalamus in patients with more frequent episodes, left and right caudate, left and right putamen, right and left pallidum signal increase detected. In the freesurfer volumetric examinations of the same 38 patients, the bilateral caudate volume increased in the group with frequent pain between both groups (Maleki *et al*., 2012). In our study, a volumetric decrease was found between the right thalamus, superior left gyrus parietalis, and left globus pallidus in migraine patients. There was no volume difference between the putamen and globus pallidus volumes. Correlation analysis showed that as the duration of migraine increased, the gray matter volume decreased in the left gyrus frontalis superior, left gyrus frontalis inferior, right gyrus precentralis, left nucleus cerebralis areas. The reason for these volumetric changes is not fully understood.

Maria A. Rocca *et al*., found gray substance increase in the dorsal aspect of the pons (Rocca *et al*., 2006). In our study, no differences were found in the areas of pons and medulla. The reason for the lack of difference in pons and medullas is that these areas contain small but rather dense neuronal structures that are thought to be different norms from other areas of the brain in imaging (Younger *et al*., 2010).

Lai TH *et al*., examined the effect of overdose on gray matter in migraine patients and found a decrease in gray matter volume in fields such as the brain frontal, temporal, occipital lobes, precuneus, and cerebellum. In our study, an increase in gray matter volume was found in these areas. It is thought that the difference in the number of patients and the difference in the radiological method used and the unknown duration of drug use may be due to the volumetric difference (Lai *et al*., 2016).

Functional imaging in patients with migraine showed activation in the posterior dorsal thalamic areas. It was suggested that these ligaments may also play a role in migraine headaches, attention deficit, transient amnesia, allodynia, phonophobia, photophobia and osmophobia (Kawasaki & Purvin 2002; Levy & Strassman 2002; Noseda & Burstein 2013; Uddman *et al*., 1985). In our study, each lobe was differentiated in more than one direction and it is thought that this differentiation may affect migrain cortical areas extensively.

Different results in different cortical areas in studies may result from different radiological methods used because individual characteristics may vary (e.g. different areas, violence, nausea more or less, lack of attention, incompetence, forgetfulness, emotionality). Differences in frontal lobes in our study may be related to functional problems such as memory problems in migraine working memory, difficulties in high mental activities, difficulty in finding words. Future clinical findings can be compared with cortical changes of these traits with the development of objectively evaluated inventories. (Aurora & Wilkinson 2007; Ayata *et al*., 2006; Coppola *et al*., 2007; Lang *et al*., 2004).

Increasing evidence suggests that increased cortical excitability is affected by migraine sensitivity (Stankewitz *et al*., 2011; Vecchia & Pietrobon 2012). Lai TH *et al*., say that cortical changes can affect treatment (Lai *et al*., 2016). In this context, our study suggests that changes in some cortical areas compared to shorter migraineurs in migraine patients with longer than 5 years are associated with increased excitability.

As a result; the use of automatic segmentation method has been shown to be easy and accurate in brain volume calculations. The presence of volumetric differences in our study is compatible with migraine pathophysiology. It is thought that volumetric changes in the different regions of the brain can affect migrain cortical areas extensively. It is thought that these properties can be compared with cortical changes by developing inventories that can objectively evaluate clinical findings in the future. It is believed that the differences in volume measurements made in migraine patients are due to method differences, number of patients included in the study, age range, duration of illness and frequency of attacks, and duration of drug use. The MR images can be helpful to guide the clinical positive / negative results of migraine patients, as well as treatment course and protocols.

Author contributions

Ö.P: Data collection, data analysis, manuscript writing and editing A.K: Literature research manuscript writing and editing N.A: Data analysis, manuscript editing I.E: Literature research Data collecting V.A.C: Data collection, manuscript writing

Conflict of interest

The authors declare no financial or other conflict of interest.

Ethical approval

The ethics approval of the ethics committee of the Technical University of the Black Sea has been granted.

Abbreviations

DICOM: Digital Imaging and Communications in Medicine
MRI: Magnetic Resonance Images
MR: Magnetic Resonance
MP: Migraine Patients
HI: Healthy Individuals
SPSS: Statistical Package for the Social Sciences
ROI: Region of Interest
VBM: voxel-based morphometry
LDDMM: Large deformation diffeomorphic metric mapping
MPRAGE: Magnetization Prepared Rapid Gradient Echo

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