DOI:10.4274/Tnd.01488

Original Article / Özgün Araştırma

Evaluation of Changes in Cerebral Structures in Migraine Patients with Diffusion and Perfusion MRI

Migrende Beyindeki Değişikliklerin Difüzyon ve Perfüzyon Manyetik Rezonans İnceleme ile Değerlendirilmesi

Ali Kemal Erdemoğlu, Ebru Kocacıklı Ocaklılar*, Sevda Yılmaz*
Kırıkkale University, Faculty of Medicine, Department of Neurology, Kırıkkale, Turkey
* Kırıkkale University, Faculty of Medicine, Department of Radiology, Kırıkkale, Turkey

Summary

Objective: The purpose of this study is to determine ischemic lesions throughout the brain parenchyma in patients diagnosed with migraine with magnetic resonance (MR) diffusion technique, evaluate vascular architecture and possible abnormalities with MR perfusion technique and to compare these values with healthy individuals within a similar age group.

Material and Method: A total of 45 migraine patients in interictal period (19 patients were diagnosed with migraine with aura) with ages between 19 and 70 (mean age 37.89±12.138) and 21 healthy volunteers with ages between 24 and 62 (mean age 36.95±13.77) were included in the study. Conventional MRI, diffusion and perfusion MRI scans were obtained.

Results: Hyperintense ischemic foci were found in 35.6% of the patients. These lesions were scattered throughout the whole brain parenchyma, with more intensity at corona radiata and the frontal lobe. No pathologic findings were found in diffusion-weighted images and there were no significant differences in ADC values between the patients and the control group (p>0.05). MR perfusion studies in migraineurs demonstrated a decrease in Cerebral Blood Flow (rCBF), prolonged Mean Transit Time (MTT) and Time to Peak (TTP) at occipital cortex, prolonged TTP at occipital white matter, centrum semiovale, cerebellum, bilateral pons, bitemporal white matter and thalamus, decreased rCBF and prolonged MTT at bilateral corona radiata, prolonged MTT at right frontal white matter, prolonged MTT and decreased rCBF and Cerebral Blood Volume (rCBV) at cerebellar cortex.

Discussion: In migraine patients, changes in cerebral vascular structures that occur as a consequence of physiopathological events during interictal periods can be evaluated with MR perfusion and MR diffusion. Further studies comparing both ictal and interictal periods are required to confirm these findings. *(Turkish Journal of Neurology 2013; 19:44-51)*

Key Words: Migraine, magnetic resonance imaging, diffusion, perfusion

Özet

Amaç: Çalışmanın amacı, klinik olarak migren tanısı almış olgularda Manyetik Rezonans (MR) Difüzyon tekniği ile beyin parenkiminde olası iskemik alanın belirlenmesi, MR Perfüzyon tekniği ile parenkimin vasküler yapısının ve olası anormalliklerinin değerlendirilmesi ve bu değerlerin benzer yaş aralığındaki sağlıklı bireyler ile karşılaştırılmasıdır.

Gereç ve Yöntem: Çalışmamıza yaşları 19 ile 70 (ortalama 37,89±12,138) arasında değişen, toplam 45 interiktal dönemdeki hasta grubu (bunların 19'u auralı migren hastası) ile yaşları 24 ile 62 (ortalama 36,95±13,77) arasında değişen, toplam 21 sağlıklı olgu kontrol grubu olarak katıldı. Konvansiyonel MR ile birlikte difüzyon ve perfüzyon ağırlıklı görüntüler alınmıştır.

Bulgular: Hastaların %35,6'sında hiperintens iskemik odaklara rastlandı. Bunlar korona radiata ve frontal lobda daha yoğun olmak üzere beyinde dağınık olarak yerleşmişti. Difüzyon ağırlıklı incelemelerde patolojik bulguya rastlanmadı; ADC değerlerinde hasta kontrol grubu karşılaştırılmasında anlamlı fark saptanmadı (p>0,05). Perfüzyon MR incelemelerinde ise migrenli hastalarda oksipital kortekste Serebral Kan Akımında (rCBF) azalma, Ortalama Geçiş Zamanı (MTT) ve Tepe Noktası için Geçen Zamanda (TTP) uzama, oksipital beyaz cevherde TTP'de uzama, her iki korona radiata düzeyinde rCBF'de azalma, MTT'de uzama ile sağ frontal beyaz cevherde MTT'de uzama, sentrum semiovalede TTP'de uzama ve ayrıca serebellumda, temporal beyaz cevherde, talamusta TTP'de uzama, serebellar kortekste MTT'de uzama rCBF ve rCBV'de azalma, pons sağ ve sol kesiminde TTP'de uzama saptandı.

Sonuç: Sonuç olarak, migrenli hastalarda interiktal dönemlerde fizyopatolojik mekanizmaların sonucunda beyindeki vasküler yapılara ait değişiklikler perfüzyon MR ve difüzyon MR incelemelerinde gözlenmistir. Bu konuda ileri çalışmaların yapılması ve iktal ve interiktal dönemlerin incelenmesi gerektiğini göstermektedir. *(Türk Nöroloji Dergisi 2013; 19:44-51)*

Anahtar Kelimeler: Migren, manyetik rezonans görüntüleme, difüzyon MR, perfüzyon MR

Address for Correspondence/Yazışma Adresi: Ali Kemal Erdemoğlu MD, Kırıkkale University, Faculty of Medicine, Department of Neurology, Kırıkkale, Türkiye Gsm.: +90 532 443 37 47 E-mail: akerdemoglu@yahoo.com
Received/Geliş Tarihi: 26.11.2012 **Accepted/Kabul Tarihi:** 27.02.2013

Introduction

Migraine is characterized with a periodic, usually unilateral, throbbing headache and affects 15-20% of individuals presenting with a headache. Migraine with aura (classic migraine) starts with neural functions, usually visual (scintillating scotoma, paresthesia, aphasia, hemiparesis), and shortly continues with headache and nausea. Although the mechanism of migraine still not clearly understood, it is known that biphasic intracerebral basal bascular constriction and following extracerebral arterial dilation is involved in the pathophysiology of migrain. Neurogenic theory defines migraine as a condition where vascular changes cause neuronal dysfunction. In addition, there is an alternative hypothesis arising from the neural mechanism in the trigeminal nerve for aura and the pain phases of migraine. This hypothesis is based on the fact that both intracranial and extracranially involved blood vessels serve trigeminovascular complex and both pain and autonomous functions innervated by small, non-myelinated fibres arising from the trigeminal nerve. The activation of these fibres releases substance P, calcitonin gene related peptide (CGRP) and other peptides into the blood vessel wall; this causes cerebral blood vessels to dilate and increase in tension. On the other hand, aura is thought to develop via CSD and accompanying arterial vasoconstriction (1,2). The decrease of cerebral blood flow in the aura stage in migraine starts in the posterior region of the brain and extends towards the anterior at a rate of approximately 25 mm per minute, based on the flow area of large arteries; it may stop at any point or may extend to the whole of the hemisphere. This is called spreading hypoperfusion, as a result of which, consistent with Leão's theory, spreading cortical neuronal depression develops.

Currently magnetic resonance imaging (MRI) provides information about the physiology of tissues with non-invasive methods that transcend anatomic and morphologic imaging. While conventional MRI scans may be normal in neurologic disorders, advanced imaging methods may be needed (3). Some of the functional physiologic imaging techniques increasing in importance are MR diffusion imaging, which is sensitive to the motion of microscopic water molecules, MR perfusion imaging that identifies tissue blood flow, MR spectroscopy based on measuring the metabolites in the brain, and brain activation mapping method BOLD (Blood Oxygenation Level Dependent Contrast) where the T2 formed by the decrease of deoxyhemoglobin caused by the increase of blood flow as a result of neuron activation and T2 contrast increase is evaluated (2,3). Diffusion weighted MR imaging is a very rapidly acquired MR imaging technique that is very sensitive to the microscopic translational (Brownian) motion of water molecules. This technique detects the signal difference resulting from the interaction of the movements of protons of water molecules in a powerful magnetic field and the absolute value of diffusion is measured on apparent diffusion coefficient (ADC) maps. In perfusion weighted imaging, the flow at capillary level is identified. This technique provides information on blood volume, blood flow, time to reach maximum for administered contrast material, mean uptake time and, indirectly, oxigenation of tissues (3).

Magnetic resonance imaging is a non-invasive technique that does not contain ionizing radiation, and that provides information on the physiologic condition of tissues beyond anatomic imaging. Diffusion and perfusion MRI, functional imaging methods, can identify hemodynamic changes that can occur in migraine patients at a microvascular level.

The purpose of this study is identifying in cases diagnosed with migraine in the clinic, possible ischemic field(s) in the brain parenchyma using MR diffusion technique, evaluating the vascular structure of the parenchyma and potential perfusion abnormalities using MR perfusion technique and comparing these results with healthy individuals of similar age groups.

Material and Method

A total of 45 interictal stage patients between the ages of 19 and 70 (36 female and 9 male) and 21 healthy control individuals between the ages of 24 and 62 (12 female and 9 male) were enrolled in the study. The patients had all presented at the Kirikkale University Medical School neurology outpatient clinic and been diagnosed with migraine based on the IHS-2004 diagnostic criteria; while 23 of the patients had unilateral headache, 19 had migraine with aura.

Patients and control subjects with diabetes mellitus, hypertension or any metabolic disease, multiple sclerosis, epilepsy, stroke, malignant condition or claustrophobia were excluded from the study.

MR Imaging

MR studies were conducted with a 1.5 Tesla MR system (Intera Master, Philips Medical Systems, Cleveland, USA) and using a standard head coil. In conventional MR scans, T1-weighted sequences (500/15; TR msn/TE msec), T2-weighted sequences (2000/125; TR msec/TE msec), FLAIR sequences (6000/120; TR msec/TE msec) in transverse plan and T1-weighted sequences (500/15; TR msec/TE msec) in sagittal plan and ve T2-weighted sequences (2000/125; TR msec/TE msec) in coronal plan were taken. Twenty segments were obtained with a segment thickness of 5 mm, intersection gap of 1 mm, field of fiew (FOV) of 230 x 80 mm and matrix of 256 x 256 mm.

EPI sequence of Philips Medical Systems was used in diffusion weighted imaging. Sequence parameters were TR/TE 7200/120, deviation angle 90°, FOV 230 x 100 mm, matrix 112 x 256 mm, slice thickness 4 mm and interslice gap 0.8 mm, and 25 axial sequences were used in 60.8 seconds. Initially T2-weighted images were obtained without using diffuwion gradient (b= 0 mm/sec), and following this, diffusion sensitive gradients were applied three dimensionally (in x, y and z axes) with a value of b = 1000 mm/sec trace images were taken by obtaining the average of the three gradients. Over the automatically generated ADC maps ADC values were measured with a mean 20±3mm region of interest (ROI) for each patient and control subject in both hemispheres in symmetrical regions. Measurements were made in frontal, parietal, temporal, occipital grey and white matter, caudate nucleus, putamen, globus pallidus, thalamus, pons, substantia nigra, red nucleus and the splenic and genu regions of the corpus callosum.

Perfusion imaging was made using T2 weighted EPI sequences with the following parameters: TE=30, FOV= 230 mm, data matrix= 256 x 256, FA= 40, slice thickness= 7 mm, gap= 0 mm. Gadopentate dimeglumine 0.2 mmol/kg (Magnevist; Berlex, Wayne, NJ) was injected from the cubital vein as contrast material with an automatic injector system (Medrad, Spectris) at a rate of

6 mL/second; following this initial injection, 20 mL saline was injected at the same rate in order to deliver the entire bolus including the contents of the connector tubes. After the administration of the contrast material, the imaging series consisting of a total of 40 image blocks were completed in approximately 1.17 minutes, and a total of 560 images were taken.

The crude images obtained were computed and TTP, MTT, TO, rCBV, rCBF measurements were taken. Measurements were made in bilateral frontal, parietal, temporal, occipital white matter, frontal and occipital grey matter, cerebellar white matter and grey matter, cerebellar peduncle, pons, substantia nigra, red nucleus, caudate nucleus, putamen, globus pallidus, thalamus and the splenic and genu regions of the corpus callosum, using $20\pm3mm^2$ round ROI.

Statistical Analysis

Data analysis was performed using SPSS 9.0 software. Continuous Verilerin analizi SPSS 9.0 paket programında yapıldı. Shapiro Wilk test was used to investigate whether continuous data distribution were consistent with normal distribution. Descriptive statistics were given as mean±standard deviation (SD) for continuous variables and percentages (%) for categoric variables.

The significance of difference for characteristics found between independent groups with measurement was evaluated with Student's t or Mann Whitney U test when the independent group number was two, and OneWay ANOVA or Kruskal-Wallis test when the independent group number was more than two. When the OneWay ANOVA or Kruskal-Wallis test statistical result was significant, post hoc tests Tukey test or Kruskal Wallis multiple comparison test was used to identify the group causing the difference. Dependent t test or Wilcoxon rank sum test was used to assess whether there was a statistically significant difference between the right and left sides within the groups. Bonferroni correction was used for intragroup comparisons.

Average age and sex distribution between groups were seen to be similar using Student's t and chi square tests, respectively. A value of $p<0.05$ was accepted as statistically significant. Results with a p value of<0.002 with the Bonferroni correction were accepted as statistically significant.

Ethics Committee

This study was approved by the Kirikkale University Medical School Ethics Committee with the approval letter dated 27/02/2006 and no 2006/056. Following the verbal informed consent process, all subjects completed written informed consent forms and provided consent.

Results

Forty-five patients between the ages of 19 and 70 (mean age 37.89±12.138) and 21 healthy subjects between the ages of 24 and 62 (mean age 36.95±13.77) were enrolled in our study. There was no statistically significant difference between the patients and the controls for age ($p>0.05$). Nineteen of the 45 migraine patients had migraine with aura, and 23 of all migraine patients had unilateral (right side in 10, left side in 13) pain complaint. When the conventional MRI scans of the patients and control subjects were evaluated, hyperintense foci were seen in especially T2 and FLAIR weighted sequences, and their localization and sizes were marked. Sixteen patients (35.6%) were found to have around

Table 1. Mean age distribution of control subjects and patients

	Patients n (45)	Controls n (21)
Age	37.89±12.14	36.95±13.77
Aura	19	
Headache side	23 unilateral	

Table 2. Distribution of ischemic gliotic foci in conventional images in the patient group, percentage

	Number	Percentage
Ischemic gliotic focus in MRI (+)	16	35.6
Ischemic gliotic focus in MRI (-)	29	64.4
Total	45	100

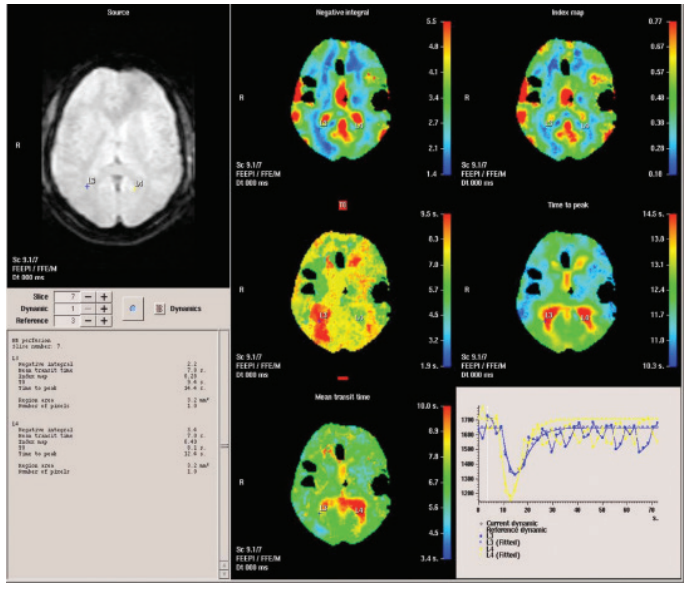

Image 1: Lengthening in MTT, TO in occipital white matter and decrease in rCBF in a patient with migraine with aura

17 hyperintense signal changes consistent with ischenic/gliotic foci, all of them smaller than 5 mm. No ischemic/gliotic foci were found in the control subjects.

Diffusion trace images and ADC maps

Abnormally increased or decreased water diffusion was not found in the visual control of diffusion trace imaging and ADC mapping. ADC values were measured symetrically in the frontal, parietal, temporal and occipital grey and white matter, caudate nucleus, putamen, globus pallidus, thalamus, pons, substantia nigra, and red nucleus. These values were not statistically significantly different between the patient and control groups (Table 4).

Evaluation of perfusion weighted images

All patients and control subjects had rCBV, rCBV mapping and MTT, TTP and TO measurements taken to evaluate perfusion weighted images. Values measured in the same localization in the patient and control groups were compared statistically (Tables 4, 5) and values where $p<0.025$ with a Bonferroni correction

was considered significant. The percentage increase/decrease of changes in localization was estimated where there was a significant difference.

Compared to the control group, there was an increase of 20.86% in the right side of pons, 27.69% in the left side of pons, 29,43% in the right thalamus, 20.69% in the right corona radiata, 24.85% in the left cerebellar cortex, 14.12% in the left cerebellar whit matter, and 31.36% in the right frontal white matter, in the patient group, in MTT, whereas the increase in TTP was 13.85% in the right cerebellum, 15.11% in the left cerebellum, 12.44% in the right side of pons, 14.29% in the right thalamus, 29% in the left thalamus, 11.39% in the right corona radiata, 12.06% in the right centrum semiovale, 11.54% in the left cerebellar cortex, 13.82% in the right occipital cortex, and 14.32% in the left occipital cortex.

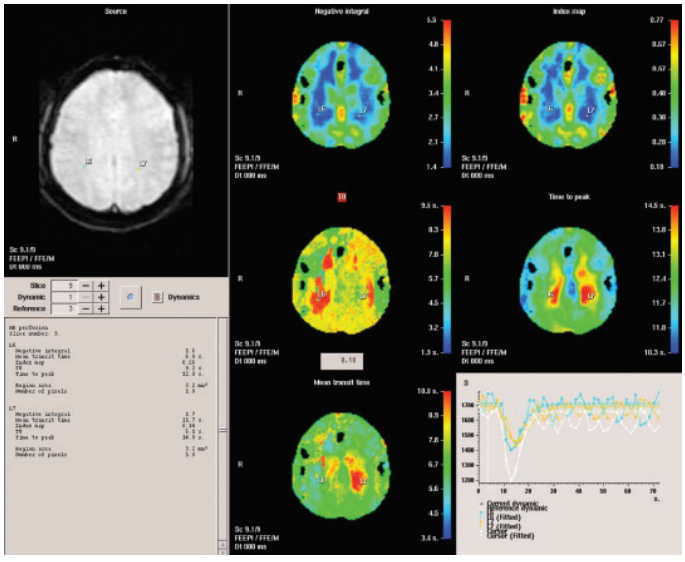

Image 2: Lengthening in MTT in left centrum semiovale in a patient with migraine without aura

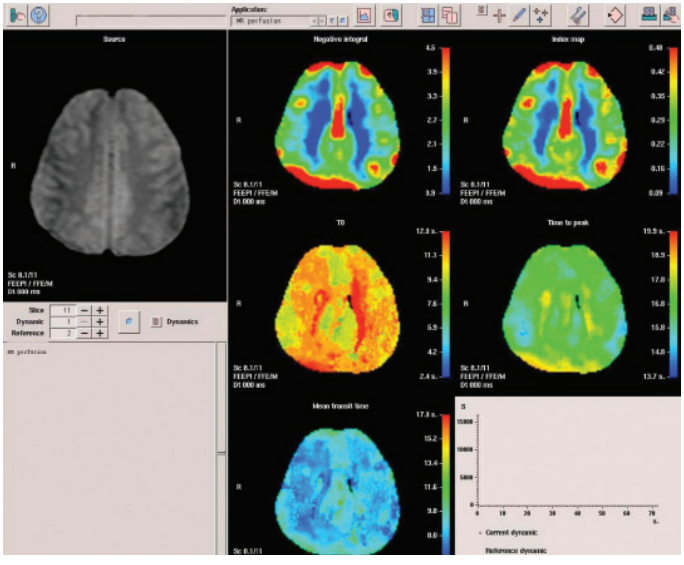

Image 3: Normal perfusion in a control subject

There was a decrease of 40.56% in the right corona radiata, 41.92% in the left corona radiata, 40.23% in the right thalamus, 24.66% in the right cerebellar cortex, 40.23 in the left cerebellar cortex in rCBF, whereas the the decrease in rCBV was 20.1% in the right corona radiata and 25.11% in the left cerebellar cortex.

As the perfusion values were symmetrically normal in the control group, symmetrical comparison of perfusion values was performed in the patient group (Tables 4, 6) (Image 3). Based on statistical results, there were significant differences between the thalamic and occipital white matter TTP, and thalamic and cerebellar cortical rCBF and rCBV (Image 1). Later multiple comparisons were made using analysis of variance between the control group and patients with and without aura, and the percentage of change was assessed in the localizations with a statistically significant difference. When the statistical results of control group and patients without aura were compared, there was an increase of 14.17% in the right temporal white matter, 16.42% in the left temporal white matter, 14.28% in the right thalamus, 29.47% in the left thalamus, 14.67% in the left corona radiata, 17.57% in the right occipital cortex, 15.99% in the left occipital cortex, 15.67% in the right centrum semiovale, 14.49% in the right cerebellar cortex, and 14.27% in the left cerebellar cortex in TTP. On the other hand, MTT showed that there was an increase of 22.6% in the right occipital cortex and 16.8% in the left occipital cortex in the patient group. There was a decrease of 20.44% in the left occipital cortex, 48.99% in the right corona radiata, and 48.75% in the left corona radiata in rCBF. Images 1 and 2 show a few of our patients. When control subjects and patients with aura were compared, there was a decrease of 18.39% in the left occipital cortex in rCBF, and it was noted that patients with decrease complained of pain on the left side. When migraine patients with and without aura were compared there were no statistically significant differences.

Table 3. Comparison of ADC values in the same localization in patient and control groups

	Control Group	Patient Group	P value
L.PONS	657.6±45.02	670.3±55.73	0.051
RightSN	760.0±51.03	720.0±63.24	0.052
L.SN	754.6±39.58	727.4±63.36	0.051
RightTEM.BC	770.1±25.09	754.8±40.93	0.06
L.TEM.BC	768.9±34.09	755.8±40.93	0.06
L.CAUD	755.4±32.84	737.7±39.80	0.051
RightGP	748.4±42.84	727.4±40.82	0.054
L.GP	764.4±39.51	738.4±41.16	0.052
SAĞKR	678.6±30.46	704.7±39.73	0.051
L.KR	685.1±37.61	713.6±34.43	0.052
RightSSO	690.3±47.93	715.5±42.32	0.051
L.OCC.BC	764.2±34.83	743.2±36.79	0.055
LOCC.KOR	760.2±34.62	739.0±34.46	0.051

Table 4. Comparison of perfusion values measured on the same side in the control and patient groups

	Control Group Mean±SD	Patient Group Mean±SD	P value
RSER.TTP	13.3±1.68	15.1±2.98	0.002†
LSER.MTT	6.5±1.32	8.2±3.10	0.020‡
LSER.TTP	12.8±1.50	14.7±2.60	0.001†
RPONS.MTT	6.5±1.08	7.9±2.09	0.010‡
RPONS.TTP	12.8±1.45	14.3±2.52	0.011†
LPONS.MTT	6.4±1.27	8.1±2.74	0.003‡
RTALA.CBF	1.8±0.51	2.7±1.12	0.002†
RTALA.MTT	5.8±0.91	7.5±2.73	0.004‡
RTALA.TTP	12.4±1.41	14.2±2.59	0.004†
LTALA.TTP	12.2±1.56	15.8±13.86	0.024†
RFRON.MTT	7.1±2.27	9.4±3.06	0.007‡
RKR.CBF	1.2±0.58	1.8±1.34	0.022**
RKR.MTT	7.1±1.40	8.5±2.83	0.024‡
RKR.CBV	0.2±0.06	0.4±0.07	0.024*
RKR.TTP	12.7±1.69	14.2±2.71	0.010†
LKR.CBF	1.2±0.57	1.7±0.76	0.007**
LKR.MTT	6.8±1.27	8.3±2.38	0.017‡
RSSO.TTP	13.7±1.61	15.3±2.82	0.024†
RSERKO.CBF	1.9±0.48	2.3±0.81	0.018**
LSERKO.CBF	1.9±0.59	2.7±0.98	0.001**
LSERKO.MTT	6.5±1.21	8.1±2.44	0.004‡
LSERKO.CBV	0.3±0.07	0.4±0.13	0.021*
LSERKO.TTP	13.1±1.45	14.6±2.55	0.003†
ROCCKO.TTP	12.9±1.59	14.7±2.75	0.023†
LOCCKO.TTP	12.9±1.61	14.8±3.17	0.024†

(Statistically significant values are specifed as CBV:* CBF:** TTP:† MTT: ‡ TO:≠.)

Discussion

Forty-five patients and 21 healthy subjects were enrolled in the perfusion and diffusion MRI study of migraine patients and there were no pathologic findings in the diffusion MR scans. There were millimetric ischemic foci localized mainly in the corona radiata and frontal white matter in 35.6% of patients (16 patients) and consistent with this, lengthening in MTT bilaterally in corona radiata, decrease in rCBF, lengthening in right corona radiata, decrease in rCBV, lengthening in right centrum semiovale TTP and lengthening in right frontal white matter MTT was found. There was bilateral lengthening in bilateral occipital cortex MTT and TTP, decrease in left occipital cortex rCBF, in addition, lengthening in right thalamic MTT, TTP, decrease in rCBF, lengthening in left thalamic TTP in the patient group. Furthermore, unlike other studies, we found lengthening in MTT and TTP in the left cerebellar cortex, decrease in rCBF and rCBV in the right cerebellar cortex, lengthening in TTP in the right cerebellar white matter, and lengthening in TTP in the right and left sides of the pons. We only enrolled interictal stage patients in this study. However, repeating ictal and interictal stage investigations of patients with and without aura and identifying individual changes may provide more optimal results.

Although the exact reason or structure of hyperintense foci seen in T2 and FLAIR conventional MRI scans is not known, it may result from neuronal and vascular events involved in the pathophysiology of migraine. Some publications claim the multiple microinfarcts that may develop as a result of causes such as platelet aggregation increase during attacks, vascular changes in migraine may be involved in the etiology of the hyperintense foci (12-47%) seen in migraineurs. In a study conducted with 91 migraine patients, ischemic gliotic foci were found in 29.4% of the patients, localized mainly in the centrum semiovale and the frontal lobe, and the basal ganglia in older patients (4). In another study, hyperintensities were found in the white matter in 16% of 185 patients (5). Pravase et al. found that 19.3% of 129 patients had focal T2 hyperintensity fields deep in the white matter and subcortical white matter (6). Osborn et al. reported that 12% of 41 patients had hyperintensities in the white matter (7). Soges et al. found that in 46% of 24 patients there were focal T2 hyperintensity fields in the white matter, cerebral and cerebellar

cortex (8). We identified hyperintense foci in 35.6% of our patients. Our findings were similar to those in the other studies. The ischemic hyperintense foci we detected in our study were localized widespread in the corona radiata, centrum semiovale and deep white matter, consistent with previously reported studies in the literature (6,7,8,9,10,11,12,13). Hyperintense multiple foci in T2 in the brain is a nonspecific finding, and seen in various conditions including multiple sclerosis, hypertensive small vessel disease (degenerative microangiopathy), vasculitis and multiple infarcts (4,5,6,7,8,9,10,11,12,13). As the incidence is reported to increase with age, migraine should be considered when these foci are detected in a young patient.

Diffusion is the random motion of molecules resulting from their thermal energy. In practice, in diffusion weighted images, the area where diffusion is restricted is seen as hyperintense because it causes slower signal loss compared to surrounding normal tissue. Diffusion weighted imaging (DWI) is most commonly used in the diagnosis of acute ischemia. Acute ischemia is seen hyperintense in DWI and hypointense in ADC mapping, whereas chronic foci are visualized as hyperisointense in DWI, and hyperintense signals in ADC mapping. In our study, there was no restriction in DWI in any of the patients and when the measured ADC values were compared with ADC values, there was no statistically significant difference. In the study conducted by Jäger et al. with 4 patients, there was no significant difference, consistent with our findings, in ADC measurements taken in visual, temporal, frontal and cortical cortex (14). In the study conducted with familial hemiplegic migraine patients, there was no diffusion pathology in a patient, but Butteriss et al. found signal increase in DWI throughout all vascular territories in the left cerebral cortex, the contralateral side of the hemiparesis in a familial hemiplegic migraine patient presenting with right hemiparesis, aphasia and headache complaints (14,15). There was no pathologic findings in the patient's follow-up MRI scan 6 months later. There are reports in literature in mainly familiar hemiplegic migraine patients that reversible restriction may occur in water diffusion in the conralateral hemisphere to the hemiparesis (16).

Changes in the cerebral hemodynamics were investigated in migraine patients because of the vascular events involved in the pathophysiology of migraine. Prior to clinical MR perfusion scans, blood flow phenomenon in migraine was investigated with radioisotope substances using intracarotid 133Xenon injection, single photon emission tomography (SPECT) and positron emission tomography (PET) methods (14). MRI is currently preferred as it does not contain radiation, has higher spatial solubility and is more easily accessible than the abovementioned methods. The principles of quantitative evaluation of hemodynamic parameters from MRI data were developed by B. Rosen et al. in 1989. This is based on the increase in concentration of contrast material being in direct proportion with decrease in T2* signal intensity (17).

Table 5. Symmetrical comparison of the right and left sides in the patient group

	Right	Left	
	Mean±SD	Mean±SD	p value
SER.CBF	1.92±0.58	2.40±1.33	0.037
SER.CBV	0.24±0.07	0.26±0.10	0.025
PONS.CBF	2.15±0.79	2.33±0.81	0.028
SUBS.TTP	13.97±2.33	13.54±2.34	0.030
TALA.CBF	2.70±2.23		0.003**
TATA.CBV	0.38±0.31		0.002*
TALA.TO	9.24±9.15		0.025
TALA.TTP	13.79±17.53		0.010†
OCC.TTP	14.79±15.54		0.013†
SERKO.CBF	2.27±2.93		0.002**
SERKO.CBV	0.30±0.39		0.001*

Statistically significant values are specified as CBV:* CBF:** TTP:† MTT: ‡ TO:≠.

Table 6. Compared change percentages in control group and migraine patients with and without aura

	Migraine without vs control	Migraine with vs control	Migraine without vs with aura
RSSO.TTP	15.67 *	6.64	8.46
RKR.CBF	48.99 *	27.90	24.31
LKR.CBF	48.74 *	31.68	12.96
RTEMPTTP	14.17 *	10.38	3.43
LTEMPTTP	16.42 *	11.25	4.65
RSERKO.TTP	14.49 *	6.10	7.91
LSERKO.TTP	14.27 *	7.44	6.36
ROCCKO.MTT	22.6 *	2.52	19.16
ROCCKO.TTP	17.57 *	8.21	8.65
LOCCKO.CBF	20.44 *	18.39 *	1.73
LOCCKO.MTT	16.88 *	7.15	9.07
LOCCKO.TTP	15.99 *	11.82	3.73

*Statistically significant.

Values obtained from perfusion measurements are regional relative values, and results compared between various areas of the brain and symmetric areas would be more accurate. In the Cutrer et al. study conducted with 4 patients with spontaneous visual aura during attacks and interictal stage, there was 6-33% decrease in rCBV, 16-53% decrease in rCBF and 10-36% increase in the occipital cortex (18). In another study conducted by the same investigators, a total of 19 patients (13 without aura) were observed during 28 migraine attacks and there was 15% and 27% decrease in rCBV and rCBF, respectively and 32% in MTT in the occipital cortex during aura; these changes were reported to continue until 2.5 hours after the onset of visual aura (19,20,21). Lagrese et al. investigated brain perfusion in 8 migraine patients with aura and 11 migraine patients without aura during ictal and interictal periods using Xenon inhalation technique and reported that there was rCBF instability in migraine patients with aura during the ictal and interictal stages (49). Lauritzen et al. found decrease in rCBF in the occipital cortex with Xenon inhalation and emission tomography in a study conducted with 11 migraine patients with aura (22). In our study, when control subjects were compared with all migraine patients, we found an increase of 13.82% in TTP in the right occipital cortex and 14.32% in TTP in the left occipital cortex. On the other hand, when control subjects and migraine patients without aura were compared, there was an increase of 17.57% in TTP and 22.6% in MTT in the right occipital cortex, 15.99% in TTP, 16.8% in MTT and 20.44% decrease in rCBF in the left occipital cortex. Finally, when we compared the control subjects and patients with aura, there was a decrease of 18.39% in rCBF in the left occipital cortes. Sanchez del Rio et al. found a perfusion defect of 10-45% in the occipital cortex and reported that values above this could cause neuronal dysfunction (18,19,20,21,22,23).

In our study, 35.6% of patients (16 patients) had millimetric ischemic foci and these foci were localized at the level of corona radiata and in the frontal lobe in 10 patients. Consistent with this, in our patient group, there was an increase of 20.69% in MTT, 11.39% in TTP, a decrease of 40.56% in rCBF, 20.1% in rCBV in the right corona radiata, increase of 22.32% in MTT, decrease of 41.92% in rCBF in the left corona radiata, increase of 15.67% in TTP in the right centrum semiovale, and increase of 31.36% in MTT in the right frontal white matter. In the 19 patient study by Sanchez del Rio et al. measurements were taken in the thalamic and temporal regions, but there were no statistically significant differences (47). On the other hand, in our study, compared to the control group there was an increase of 29.43% in MTT, 14.29% in TTP, decrease of 40.23% in rCBF in the right thalamus, and increase of 29% in TTP in the left thalamus in the patient group, but there was no significant difference in the temporal white matter.

Measurements were taken in bilateral caudate nuclei, globus pallidus, putamen, substantia nigra and red nuclei, but no statistically significant differences were found. As far as we know, there are no studies in literature reporting any pathologic findings in these regions.

Cerebellar peduncle, cerebellar white matter, cerebellar cortex, pons and splenic and genu regions of the corpus callosum have not been investigated in migraine previously. Our results show that there was an increase of 24.85% in MTT, 11.54% in TTP in the left cerebellar cortex, decrease of 24.66% in rCBF, 25.11% in rCBV in the right cerebellar cortex, increase of 14.12% in MTT, 15.11% in TTP in the left cerebellar white matter, 13.85% in TTP in the right cerebellar white matter, 12.44% in TTP in the right side of pons, 27.69% in TTP in the left side of the pons in the patient group. When measured localizations were bilaterally compared in the patient group, there was lengthening in TTP in the thalamic and occipital white matter, decrease in rCBF and rCBV in the thalamic and cerebellar cortex, relative to their symmetric sides.

The limitations of our study are the relative small sample size and lack of imaging during aura stage and attacks due to aura stage being very short.

In conclusion, perfusion MR can be used as a non-invasive method to show the hemodynamic changes that may occur in the brain in the pathophysiology of migraine, which is still not completely understood. Changes in the cerebrovascular structures occurring as a result of pathophysiologic mechanisms during interictal stages in migraine patients have been observed in perfusion MRI and diffusion MRI scans. This shows that advanced studies should be conducted and ictal and interictal stages should be investigated.

References

1. Dalkara T, Nozari A, Moskowitz MA. Migraine aura pathophysiology: the role of blood vessels and microembolisation. Lancet Neurol 2010;9:309-317.
2. Bernstein C, Burstein R. Sensitization of the trigeminovascular pathway: perspective and implications to migraine pathophysiology. J Clin Neurol 2012;8:89-99.
3. Aksoy FG, Lev MH. Dynamic contrast-enhanced brain perfusion imaging: technique and clinical applications. Semin Ultrasound CT MR 2000;21:462-477.
4. Igarashi H, Sakai F, Kan S, Okada J, Tazaki Y. Magnetic resonance imaging of the brain in patients with migraine. Cephalalgia 1991;11:69-74.
5. Cooney BS, Grossman RI, Farber RE, Goin JE, Galetta SL. Frequency of magnetic resonance imaging abnormalities in patients with migraine. Headache 1996;36:616-621.
6. Pavese N, Canapicchi R, Nuti A, Bibbiani F, Lucetti C, Collavoli P, Bonuccelli U. White matter MRI hyperintensities in a hundred and twenty-nine consecutive migraine patients. Cephalalgia 1994;14:342-345.
7. Osborn RE, Alder DC, Mitchell CS. MR imaging of the brain in patients with migraine headaches. AJNR Am J Neuroradiol 1991;12:521-524.
8. Soges LJ, Cacayorin ED, Petro GR, Ramachandran TS. Migraine: evaluation by MR. AJNR Am J Neuroradiol 1988;9:425-429.
9. Cooney BS, Grossman RI, Farber RE, Goin JE, Galetta SL. Frequency of magnetic resonance imaging abnormalities in patients with migraine. Headache 1996;36:616-621.
10. Tortorella P, Rocca MA, Colombo B, Annovazzi P, Comi G, Filippi M. Assessment of MRI abnormalities of the brainstem from patients with migraine and multiple sclerosis. J Neurol Sci 2006;244:137-141.
11. Gozke E, Ore O, Dortcan N, Unal Z, Cetinkaya M. Cranial magnetic resonance imaging findings in patients with migraine. Headache 2004;44:166-169.
12. Ziegler DK, Batnitzky S, Barter R, McMillan JH. Magnetic resonance image abnormality in migraine with aura. Cephalalgia 1991;11:147-150.
13. Jäger HR, Giffin NJ, Goadsby PJ. Diffusion- and perfusion-weighted MR imaging in persistent migrainous visual disturbances. Cephalalgia 2005;25:323-332.
14. Butteriss DJ, Ramesh V, Birchall D. Serial MRI in a case of familial hemiplegic migraine. Neuroradiology 2003;45:300-303.
15. Obendorfer S, Wober C, Nasel C, Asenbaum S, Lahrmann H, Fueger B, Grisold W. Familial hemiplegic migraine: follow-up findings of diffusion-weighted magnetic resonance imaging (MRI), perfusion-MRI and [99mTc] HMPAO-SPECT in a patient with prolonged hemiplegic aura. Cephalgia 2004;24:533-9.

16. Grant PE, He J, Halpern EF, Wu O, Schaefer PW, Schwamm LH, Budzik RF, Sorensen AG, Koroshetz WJ, Gonzalez RG. Frequency and clinical context of decreased apparent diffusion coefficient reversal in the human brain. Radiology 2001;221:43-50.
17. Rosen BR, Belliveau JW, Vevea JM, Brady TJ. Perfusion imaging with NMR contrast agents. Magn Reson Med 1990;14:249-265.
18. Cutrer FM, O'Donnell A, Sanchez del Rio M. Functional neuroimaging: enhanced understanding of migraine pathophysiology. Neurology 2000;55(Suppl 2):36-45.
19. Huisman TA, Sorensen AG. Perfusion-weighted magnetic resonance imaging of the brain: techniques and application in children. Eur Radiol 2004;14:59-72.
20. Edelman RR, Mattle HP, Atkinson DJ, Hill T, Finn JP, Mayman C, Ronthal M, Hoogewoud HM, Kleefield J. Cerebral blood flow: assessment with dynamic contrast-enhanced T2*-weighted MR imaging at 1.5 T. Radiology 1990;176:211-220.
21. Sanchez del Rio M, Bakker D, Wu O, Agosti R, Mitsikostas DD, Ostergaard L, Wells WA, Rosen BR, Sorensen G, Moskowitz MA, Cutrer FM. Perfusion weighted imaging during migraine: spontaneous visual aura and headache. Cephalalgia 1999;19:701-707.
22. Lauritzen M, Olesen J. Regional cerebral blood flow during migraine attacks by Xenon-133 inhalation and emission tomography. Brain 1984;107:447-461
23. Lagrèze HL, Dettmers C, Hartmann A. Abnormalities of interictal cerebral perfusion in classic but not common migraine. Stroke 1988;19:1108-11011.