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The value of EEG and SPECT in the assessment of juvenile migraine

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Abstract

Despite the cause of migraine headaches is not exactly understood, cerebral blood flow studies revealed new insights in the pathophysiology of migraine. The data from Single Photon Emission Computerized Tomography studies in juvenile group diagnosed according to the HIS criteria are very rare, also there are limited number of studies in literature in which SPECT and EEG findings are combined. This study aimed to evaluate changes in regional cerebral blood flow and EEGs in juvenile patients suffering from migraine, also to investigate the relationship between SPECT and EEG in respect to comparison of each other, the frequency of attacks and response to the treatment. We grouped 20 children with migraine, 9 with aura, 11 without aura, and obtained SPECT and EEG's in ictal and interictal periods. All patients received Propranolol after the studies were performed. Regional cerebral and cerebellar perfusion was evaluated both visually and semiquantitatively. In the study, visual observation of SPECT revealed that perfusion defect was found 88% for ictal, 55% for interictal period and 55% for ictal, 18% for interictal period in patients with and without aura, respectively. The corticocerebellar ratios obtained semiquantitativly revealed significant differences between ictal and interictal periods in patients without aura, ictal periods in patients with and without aura, interictal periods in patients with and without aura. EEG findings were not significant. All patients who received therapy recovered well. Overall, SPECT can be used as an additional test for diagnosis of migraine because it is useful for visualization of perfusion defect especially in ictal and interictal periods with aura, and in ictal period without aura in childhood. These finding suggest that the idea of the origins of migraines with or without aura might be similar. It is necessary to investigate in large series in order to clarify the pathogenesis of the disease further.

Keywords: juvenile migraine, eeg, spect, headache

1. Introduction

Despite many studies, pathogenesis of migraine is not completely understood and none of the theories proposed has gained certainity. Vascular and neuronal theories have been discussed in terms of apparent clinical and pathological resemblances. Inasmuch as vascular theory couldn't explain the whole migraine mechanism, it is supplemented by neuronal theory (1). The best studied phenomenon of migraine attack is the cortical spreading depression (CSD) pattern of Leao. This disturbance of the cerebral cortical function is associated with metabolic and haemodynamic changes which have been described well in some studies (2). It may be notified that migraine attacks occur with respect to exacerbations of preexisting changes in cerebral autoregulation due to innate or exogenous factors (3).

With the advances, regional cerebral blood flow (rCBF) studies revealed new insights into the pathophysiology which some showed hypoperfused areas especially in migraine patients with aura during interictal (3-6, 8-13) and ictal period (5-8), while others showed only nonspecific changes (4, 8, 14) or even hyperperfused areas (4, 6).

One of the relatively new techniques that describe cerebral blood perfusion alterations is Tc-99m HMPAO Single Photon Emission Computerized Tomography (SPECT), which the data in juvenile age group is very rare. Likewise EEG is one of the most commonly used neurophysiological method intended for migraine pathophysiology. That being said, to the best of our knowledge, there is no study combining both SPECT and EEG findings in juvenile migraine group diagnosed according to the International Headache Society (HIS) criteria in order to determine possible ictal and interictal vascular and electrophysiologic changes.

The aim of our study was to evaluate changes in rCBF and EEG's in juvenile patients suffering from migraine with aura ((MwA) and without aura (MwoA), also to investigate the relationship between SPECT and EEG in respect to comparisons of each other, the frequency of attacks and response to the treatment.

2. Materials and Methods

The study involved 20 juvenile patients, 9 with aura (mean age±sd: 13.5±2), 11 without aura (mean age±sd: 12.3±3) with the diagnosis of migraine who admitted to the Department of Pediatric Neurology in the Ondokuz Mayıs University School

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of Medicine between 1999 and 2000. Juvenile migraine was diagnosed on the basis of headache classification of the IHS. Patients with history of migraine lasting from at least a year who do not receive any prophylactic drugs other than propranolol (which stopped at least 3 months prior to the assessment) were included. Children who had abnormalities on neurologic examination and intracranial structural defects were excluded. Patients were also divided into three groups according to the attack frequency: ≤5 attact/month; 6-10 attact/month; >10/month. Propranolol treatment (1 mg/kg/day) has been given to all the patients after the study was performed.

Treatment response was evaluated at the third and sixth months of follow-up visits. SPECT and EEG studies were performed during headache free (interictal) and headache (ictal) periods to all patients during both ictal (in the first six hours after the headache had begun) and interictal periods (at least 24 hours for SPECT and 72 hours for EEG studies after the attack had stopped). Blood flow measurements were carried out by SPECT. A single head gamma camera (GE, starcam 4000i XCT, WI USA) fitted with a low energy high resolution collimator was used. Fifteen minutes after the bolus injection of Tc-99m HMPAO at a dose of 18,5 MBq/kg into the vein, brain acquisitions were collected. Cerebellar activity was chosen to normalize the brain slices. Cortico-cerebellar ratios (CCRs) were estimated by dividing the mean values detected from 10 different areas of the brain to ipsilateral cerebellum values. Transaxial slices parallel to orbitomeatal line were used to determine perfusion index (PI) of total 17x2 brain regions. The rectangular regions of interest (ROIs) (5x5 pixel) were set on the brain regions while irregular ROIs were drawn over the cerebellar hemisphere (Fig. 1).

EEGs were recorded at least for 20 minutes. The Wilcoxon test was used to compare the mean PI values. The Mann-Whitney U test was used to compare the mean PI values for ictal and interictal images in patients with and without aura. Evaluations within the groups were performed by paired-t test, between the groups by Student-t test. In our study, SPECT and EEG findings were interpreted with each other, frequency of attacks and response to the treatment by using chi-squared test, Fisher's exact test and Mc Nemar test. All the evaluations were performed by the same nuclear medicine specialist.

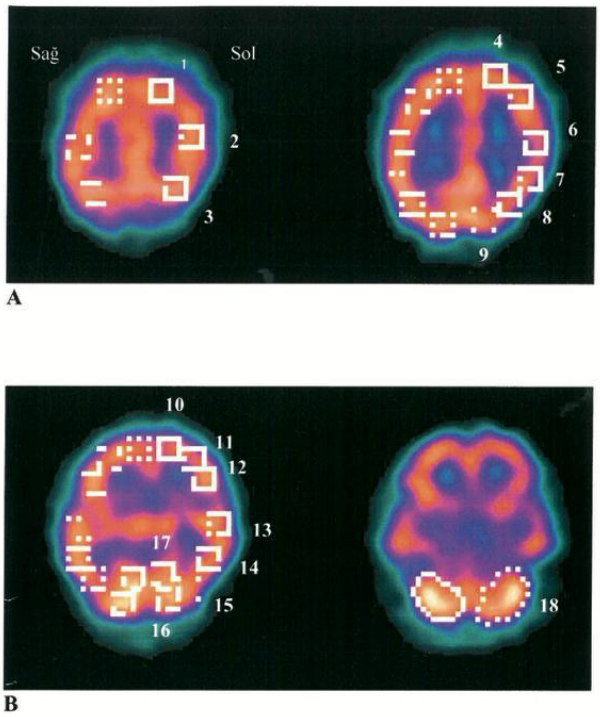

Fig 1 (A, B). Distribution of regions of interest (ROIs) used in semiquantitative evaluation according to the section. (1) Sup. Frontal 1, (2) Paracentral 1, (3) Sup. Parietal 1, (4) Sup. Frontal 2, (5) Middle Frontal 1, (6) Paracentral 2, (7) Sup. Parietal 2, (8) Inf. Parietal, (9) Cuneus, (10) Sup. Frontal 3, (11) Middle Frontal 2, (12) Inf Frontal, (13) Sup. Temporal, (14) Middle Temporal, (15) Occipital, (16) Occipital pole, (17) Visual cortex, (18) Cerebellum

3. Results

3.1. Patients and Study Design

General characteristics of study patients are given in Table 1. A total of 20 children, 11 girls (55%) and 9 boys (45%) aged 7 years to 16 years were included. Of the 20 patients, 9 had MwA (3 female, 6 male) and 11 (8 female, 3 male) had MwoA. The mean ages of cases with or without aura were 13,5±2 years (11-16) and 12,3±3 (7-16) years respectively. Attack frequency was less than 5 per month in half of the cases while it was 6-10 in 7 and greater than 10 in 3 patients. Half of the patients had unilateral headache. All of the patients with aura had visual symptoms. Neurologic symptoms were compatible with perfusion defect in 5 of 9 migraine patients with aura. Brain Computed Tomography (CT) was normal which was obtained in 7 patients.

Table 1. Clinical characteristics of patients

Patient number	Gender	Age (year)	Type of migraine	Period of illness (year)	Family history	Attack frequency	Attack duration	Headache localization	Associated neurological symptoms
1	G	16	W aura	2	+	3-4/m	1 d	Bil.O.F.	teichopsia, photopsy
2	B	15	W aura	1,5	Ø	4/m	1-2 d	Uni.O.	Teichopsia, blurred vision
3	B	13	W aura	1	Ø	1-2/m	3-4 h	Bil.F.	fortification
4	G	11	W aura	1	Ø	8-10/m	3-4 h	Uni.F.P.	photopsy scotoma
5	G	13	W aura	1	Ø	7-8/m	3-4 h	Uni.O.P.	Teichopsia, photopsy

6	B	11	W aura	1	+	7-8/m	2-3 h	Bil.O.	photopsy, scotoma
7	B	15	W aura	1	Ø	3/w	2-3 h	Bil. O.F.	blurred vision
8	B	12	W aura	2-3	Ø	3/w	3-4 h	Uni. F.	photopsy
9	B	16	W aura	4	Ø	1-2/m	1-2 d	Bil. F.	photopsy, scotoma
10	G	16	w/o aura	1,5	+	1-2/m	1 d	Uni. F.	
11	G	16	w/o aura	1,5	Ø	3/m	1 d	Uni. F. P.	
12	G	9	w/o aura	3-4	Ø	1/m	1-2 d	Uni.P. T.	
13	G	10	w/o aura	1	+	7-8/m	3-4 h	Bil. F.	
14	B	10	w/o aura	2	+	1/m	1-2 d	Uni. F.	
15	B	7	w/o aura	1	Ø	1/m	3-4 h	Bil. F.	
16	G	13	w/o aura	1	+	8-10/m	3-4 h	Uni. F. P.	
17	B	15	w/o aura	3	+	4-5/m	1 d	Bil. F.	
18	G	14	w/o aura	3	Ø	10/m	3-4 h	Bil. F.	
19	G	12	w/o aura	2	+	3/w	3-4 h	Bil. F.	
20	G	14	w/o aura	1,5	+	7-8/m	5-6 h	Bil. F. P.	

3.2. SPECT Findings

SPECT findings obtained by visual evaluations are given in Table 2. Out of 9 patients with aura, 8 (88%) showed perfussion defect during ictal period with 11,7% in pariatal lobe, 9,1% in frontal which was bilateral in 3 patients. Decreased rCBF was observed in all brain lobes. Images of hypoperfused areas during ictal period obtained from Patient 3 are shown in Fig. 2A, as for Patient 9 in Fig. 3A. In the group with aura, while perfusion defect during interictal period continued in 5 of the 9 cases (55%), it had normalized in other 4 patients. In Patient 3, hypoperfused areas were converted to normal in interictal period (Fig. 2B). Patient 9 showed continuation of ictal hypoperfused areas in interictal period as well, with relative increase in blood perfusion (Fig. 3B).

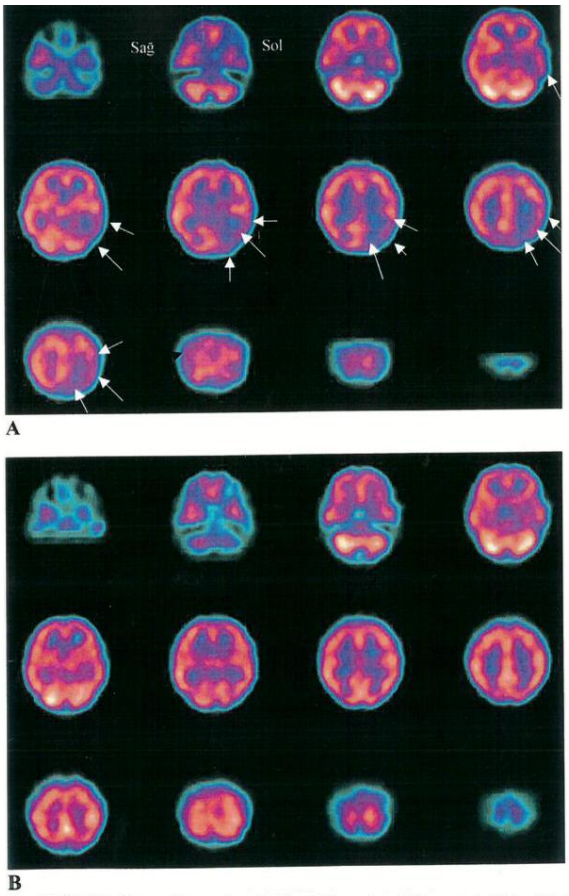

Fig. 2 (A,B). In Patient 3, hypoperfusion was observes in left parietal, temporal and occipital areas during ictal stage (A) with axial section by Tc-99m HMPAO SPECT. During interictal stage (B), braib perfusion was normal

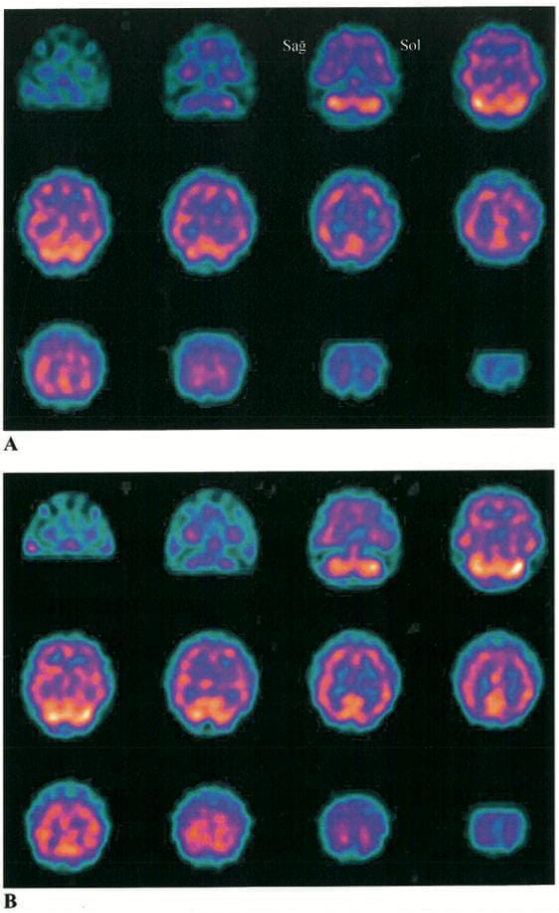

Fig. 3 (A, B). In Patient 9, widespread hypoperfusion was observed in the brain during ictal stage (A) with axial section by Tc-99m HMPAO SPECT. The same patient showed continuation of ictal hypoperfused areas in interictal period as well, with relative increase in blood perfusion (B)

Table 2. SPECT and EEG results obtained by visual evaluations

	Perfused areas		EEG		Relationship of perfusion to symptoms	CT
n	Ictal	Interictal	Ictal	Interictal	+	Not available
1	Bil. P.O.↓	Normal	Normal	Normal	+	Normal
2	Left F.P.T.O↓ RightO.↓	Left T.O.↓ Right O.↓	Voltage supression	Normal	+	Normal
3	Left P.T.O↓	Normal	Voltage supression	Normal	∅	Normal
4	Left F.P.T.↓	Normal	Normal	Normal	∅	Not available
5	Left F.P.↓ Right F.T↓	Bil.P.↓	Normal	Normal	∅	Not Available
6	Normal	Normal	Normal	Normal	∅	Normal
7	Left F.P.O.↓ Right F.↓	Left F. ↓	Normal	Normal	+	Not available
8	Bil. P.↓	Bil.P.↓	Voltage supression	Voltage supression	∅	Not available
9	Bil. F.P.T.O↓	Bil.F.P.T.O↓	Normal	Normal	+	Normal
10	Right P↓ Left P.T.O.↓	Right F.P↓ Left F.P.T.O↓	Normal	Normal		Not available
11	Bil. P.↓ Bil. F. ↑	Normal	Normal	Normal		Not available
12	Normal	Normal	Normal	Normal		Not availabl
13	Normal	Normal	Normal	Normal		Normal
14	Normal	Normal	Voltage supression	Voltage supression		Not available
15	Normal	Normal	Voltage supression	Normal		Not available
16	Normal	Normal	Normal	Normal		Normal
17	Bil.T.P.O↓	Normal	Normal	Normal		Not available
18	Bil.P.↓	Normal	Normal	Normal		Not available
19	Bil. P↓ Bil. O.↑	Bil.P.↓	Voltage supression	Normal		Not available
20	Left F.P.↓	Normal	Normal	Voltage supression		-

F:Frontal, P:Parietal, O:Occipital, T:Temporal, Bil: Bilateral, +:associated, ∅: nonassociated

In the group without aura, hipoperfusion were observed in 6 of 11 patients (55%) during ictal period. Regional CBF was reduced mainly in the parietal lobe. Slightly hyperperfused areas were observed in 2 patients as well (patient 11 and 19). Perfusion defect was bilateral in 5 patients. In interictal period, normal perfusion was observed in 4/6 while 2 patients still had hypoperfused areas. While one patient (Patient 10) showed new hypoperfused areas additional to the areas seen in ictal period, the other (Patient 19) had lesions to continue regressively.

Table 3. Mean perfusion indexes (PI) (SD) during the ictal and interictal phases in migraineurs with aura and without aura

	With Aura (n: 18)		Without Aura (n:22)					
	Ictal (Mean±SD)	Interictal (Mean±SD)	Ictal (Mean±SD)	Interictal (Mean±SD)	P1	P2	P3	P4
Sup. Frontal 1	0.96±0.07	0.98±0.08	1.02±0.09	1.03±0.07	≠	≠	*	≠
Paracentral 1	0.95±0.09	0.97±0.07	0.96±0.06	1.01±0.08	≠	**	≠	≠
Sup. Parietal 1	0.89±0.10	0.93±0.06	0.91±0.09	1.00±0.07	*	***	≠	≠
Sup. Frontal 2	0.93±0.07	0.91±0.07	1.02±0.09	0.99±0.07	≠	≠	**	**
Middle Frontal1	0.94±0.07	0.94±0.08	1.02±0.07	1.01±0.07	≠	≠	***	**
Paracentral 2	0.92±0.10	0.94±0.08	0.97±0.07	0.99±0.07	≠	≠	≠	≠
Sup. Parietal 2	0.93±0.11	0.94±0.06	0.96±0.07	0.98±0.05	≠	≠	≠	≠
Inf. Parietal	0.84±0.11	0.86±0.05	0.85±0.08	0.93±0.09	≠	**	≠	*
Cuneus	0.94±0.12	0.97±0.05	1.01±0.10	1.02±0.09	≠	≠	*	≠
Sup. Frontal 3	0.84±0.08	0.87±0.10	1.00±0.11	0.95±0.06	≠	≠	****	**
Middle Frontal 2	0.89±0.08	0.90±0.08	1.01±0.09	0.98±0.08	≠	≠	****	*
Inf. Frontal	0.91±0.06	0.92±0.07	0.98±0.07	0.96±0.08	≠	≠	***	*
Sup. Temporal	0.95±0.09	0.96±0.07	1.00±0.07	1.00±0.08	≠	≠	*	≠
Middle Temporal	0.91±0.09	0.93±0.07	0.94±0.08	0.97±0.07	≠	≠	≠	*
Occipital	0.91±0.10	0.93±0.07	0.95±0.07	0.97±0.09	≠	*	≠	≠
Occipital Pole	1.03±0.07	1.03±0.06	1.08±0.07	1.10±0.07	≠	≠	≠	≠
Visual Cortex	0.94±0.07	0.97±0.05	1.00±0.07	1.04±0.07	≠	**	*	≠

*p<0.05, ** p<0.01, *** p<0.001, , **** p=0.000, ≠p>0.05 **P1**: Comparison of PI values between ictal and interictal phases in patients with aura. **P2**: Comparison of PI values between ictal and interictal phases in patients without aura. **P3**: Comparison of ictal PI values between patients with and without aura. **P4**: Comparison of interictal PI values between patients with and without aura.

When SPECT results were evaluated by CCR scale (Table 3), statistically significant difference was observed only in superior parietal 1 area between ictal and interictal periods in MwA (p<0,05) while it was observed in paracentral, inferior parietal and visual cortex (p<0,01) with the highest significance in superior parietal area (p<0,001) in cases

without aura. When it was evaluated between migraine patients with and without aura ictally, statistically significant differences were obtained in frontal area, cuneus, superior temporal and visual cortex with the highest significance in superior and middle frontal areas (p=0.000) while it was observed significant in frontal area during interictal period (p<0.01).

When evaluating ictal and interictal SPECT findings among whole patients (Table 4), data comparing areas with normal perfusion and hypoperfusion qualitatively during ictal period showed that there was significance only in the areas of superior parietal 1 and superior frontal 3 (p<0,05).

Table 4. Mean perfusion indexes (PI) (±sd) during ictal and interictal phases comparing areas with normal perfusion and hypoperfusion

		Ictal			Interictal					
	n	Hypoperfused (Mean±SD)	n	Normal	n	Hypoperfused (Mean±SD)	N	Normal (Mean±SD)	P1	P2
Sup. Frontal 1	2	0.81±0.05	36	1.00±0.08	2	0.90±0.05	38	1.02±0.07	≠	Ø
Paracentral 1	5	0.86±0.06	35	0.96±0.07	2	0.94±0.03	38	1.00±0.08	≠	Ø
Sup. Parietal 1	11	0.79±0.06	29	0.94±0.07	4	0.85±0.02	36	0.98±0.07	*	****
Sup. Frontal 2	2	0.77±0.05	38	0.99±0.09	2	0.85±0.02	38	0.96±0.08	≠	Ø
Middle Frontal1	2	0.80±0.03	38	0.99±0.08	2	0.87±0.05	38	0.98±0.07	≠	Ø
Paracentral 2	3	0.78±0.00	37	0.96±0.08	2	0.86±0.07	38	0.97±0.07	≠	Ø
Sup. Parietal 2	6	0.83±0.07	34	0.97±0.08	2	0.93±0.02	38	0.96±0.06	≠	Ø
Inf. Parietal	7	0.77±0.07	23	0.90±0.06	9	0.83±0.03	31	0.91±0.08	≠	****
Cuneus	7	0.76±0.03	31	0.10±0.05	2	0.92±0.03	38	1.00±0.08	≠	Ø
Sup. Frontal 3	9	0.78±0.07	31	0.98±0.10	2	0.74±0.05	38	0.93±0.08	*	Ø
Middle Frontal2	7	0.81±0.05	33	0.99±0.09	3	0.81±0.04	37	0.96±0.08	≠	Ø
Inf. Frontal	4	0.81±0.04	36	0.96±0.06	4	0.85±0.05	36	0.95±0.07	≠	Ø
Sup. Temporal	4	0.84±0.07	36	1.00±0.07	3	0.90±0.02	37	0.99±0.08	≠	Ø
Middle Temporal	8	0.84±0.03	32	0.96±0.08	4	0.86±0.02	36	0.96±0.07	≠	Ø
Occipital	8	0.82±0.04	32	0.97±0.07	2	0.83±0.06	38	0.97±0.08	≠	Ø
Occipital Pole		--	40	1.06±0.09		--	40	1.07±0.07	≠	Ø
Visual Cortex	3	0.85±0.01	37	0.98±0.08	1	0.89±00	39	1.01±0.07	≠	Ø

*p<0.05, **** p=0.000, ≠p>0.05, Ø no statistical analysis has been made. **P1**: Comparison of PI values qualitatively obtained from normal perfused areas between ictal and interictal phases. **P2**: Comparison of PI values qualitatively obtained from hypoperfused and normal perfused areas during ictal phases.

3.3. EEG Findings

EEG findings are given in Table 2.

Voltage suppression was present in 3/9 patients (33%) in ictal, 1/9 (11%) in interictal period in patients with aura and 3/11 patients (27%) in ictal, 2/11 (18%) in interictal period in patients without aura, as within the same patient**.**

Comparison of SPECT and EEG data in patients with and without aura in ictal and interictal periods:

Out of 10 patients whose attack frequency 1-5/month in ictal period, 4 patients with aura showed perfusion defect in their SPECT (100%) and half of them had voltage suppression in their EEG (50%); out of the rest of 6 patients without aura, 3 showed perfusion defect in their SPECT (50%) and one third had voltage suppression in their EEG (33%). Analyzing 7 patients whose attack frequency 6-10/month in ictal period, 1 patient out of 3 with aura showed perfusion defect in their SPECT (33%), none showed voltage suppression in EEG (0%); half of 4 patients without aura (%50) showed perfusion defect in SPECT (50%) with none had voltage suppression in EEG (0%). When examined 3 patients with an attack frequency of 10 or more /month in ictal period, both two patients with aura had perfusion defect in SPECT (%100), one of them had voltage suppression in EEG. When compared whole patient's SPECT and EEG findings and attack frequency with each other, there was no statistical significance (p>0.05).

When evaluating response to propranolol treatment (1 mgr/kg/day), 18 patients out of 20 gave response to 3 or 6 months of medication. There was no statistical difference in patients with or without aura in relation to the treatment response with cerebral perfusion defect and their EEG (p>0.05).

4. Discussion

Migraine is a vascular disease which pathophysiology is not understood clearly in spite of several studies. Cerebral blood flow studies performed over the years have brought a new dimension to the debate. Studies combining SPECT and EEG findings in migraine patients with and without aura are limited and very few of them are in juvenile age group diagnosed according to the HIS criteria.

Cerebral perfusion studies performed in patients with and without aura in ictal and interictal periods are vary. Although early rCBF studies in the ictal phase in patients with MwA shows hyperperfusion, especially some studies performed with PET and SPECT have shown a pattern of reduced rCBF during the headache phase (4-7). Olesen J et al (6) studied in 63 migraineous patients with aura during the aura phase, headache phase and after the headache disappeared, and showed that the first observed event was a decrease in regional cerebral blood flow in the posterior of one cerebral hemisphere. The development of this process was accompanied by aura symptoms, followed by headache while the rCBF remained

low. In the headache phase, the CBF increased gradually from low to abnormally high while headache was disappeared in some patients. In the study of Soriani et al (4), perfusion abnormalities were found in 14 of 19 patients in the ictal period in patients with aura, of which 11 was hypoperfusion. In Lauritzen and Olesen's SPECT series of 33 patients with Xe-133 inhalation (7), unilateral hypoperfusion was found in 8 out of 11 in patients with aura during the attack. Studies performed in migraine patients during interictal period are substantially more. Even though normal perfusion studies of Xenon-133 and SPECT performed in MwA in interictal period were rarely reported (4, 15), studies with abnormal perfusion pattern were published (3-6, 9-13). In the interictal SPECT study of Battisella et al (8) on 19 juvenile migraineurs with and without aura, none of 10 patients without aura showed perfusion defect while hypoperfused areas were found in 4 out of 9 patients with aura and they suggested that insufficient regional cerebral vascular autoregulation may occur even in the interictal period in patients with classical and hemiplegic migraine. Schlake et al (3) detected hypoperfusion in 19 out of 23 adult patients with MwA during interictal period in their SPECT study and stated that the most significant change was in a patient with complicated migraine. In the SPECT study of Calamussi (12) in patients with aura, perfusion disorders were shown in 22 out of 28 patients during interictal period and concluded that SPECT is useful in the diagnosis of migraine. Maini et al (13) found decreased rCBF in their SPECT study in 13 of 14 patients with aura during interictal period. Contrary, in the brain SPECT study of Tc.09m HMPAO performed by Soriani et al (4) in a 30-person group of patients with juvenile MwA (19 in the ictal and interictal period, 11 in the interictal period only), hypoperfusion was found in 4 of 20 patients and normal perfusion in 16 of them in interictal period.

In our study, a significant decrease in cCBF was detected in the in ictal period in the majority of migraineurs with aura (%88). Decreased cCBF was observed in all brain lobes. In interictal period of 3/9 patients, rCBF had normalized while 5 others (%55) still showed hypoperfusion and continued with a decrease in number and width of the defects. Therefore, despite higher corticocerebellar ratios (CCRs) of 15 out of 17 brain regions, significant difference was not found between ictal and interictal brain perfusion by semicantitative evaluation (Table 3). The findings we obtained in interictal period in patients with aura are consistent with the literature (3-6, 9-13). In spite of limited number of studies conducted in the ictal period, our findings show consistency to some studies (4-7).

Although most of the studies conducted in the interictal period in MwoA found normal flow pattern (8, 11, 14), one large-series of SPECT study with Xe-133 inhalation showed significant asymmetry (15). Ferrari et al (14) did not observe significant regional cerebral perfusion asymmetry in the attack-free period, during the attack, and after the treatment with Sumatriptan in the Tc-99m HMPAO SPECT performed in a group of 20 patients with MwoA. In the interictal SPECT study conducted in 29 adult patients (24/29 migraineus without aura) by Mirza et al (9) revealed significantly reduced Tc 99m-HMPAO uptake in the right lower frontal, temporal, upper frontal and occipital regions. In Levin et al's interictal study (16), rCBF values measured by 133Xe inhalation were lower in migraineurs than in controls. Mean asymmetry index of the classic/complicated group was significantly higher than that of the controls but not different from that of the common migraine group. It was suggested that in the headache-free interval rCBF asymmetries exist in classic/complicated migraineurs variable in location and may be related to the cause or the effect of the focal neurologic dysfunction that occurs during an attack in these patients.

Despite early studies characterized hyperemia as occurring during the ictal phase of MwoA, large series studies conducted subsequently have revealed normal global or regional CBF (7, 14, 15). A normal cerebral blood flow pattern was observed in all 12 individuals with MwoA during the attack in Lauritzen and Olesen's SPECT series (7) of 33 patients with Xe-133 inhalation. Bednarczyk et al (17) used PET to quantify global CBF, oxygen metabolism, and oxygen excretion in a group of 9 participants and discovered that CBF was reduced throughout the headache phase. Cerebral oxygen metabolism and excretion remained severely diminished.

In our study, ictal hypoperfused areas were seen in 55% of patients without aura. Regional CBF was reduced mainly in the parietal lobe. Two patients showed slightly hyperperfused areas in addition to hypoperfused regions. Perfusion recovered to normal in 4 of 6 patients during the interictal period, while remained low in 2/6. This restoration to normalcy in brain perfusion observed during the interictal phase was confirmed semiquantitatively (ictal-interictal comparison) in 5 of 17 brain areas in CSO values (Table 3). It was shown that two individuals with MwoA (patients 11 and 19) exhibited both hyper and hypoperfused brain regions (bilateral frontal in patient 11 and bilateral occipital in patient 19).

Our findings in the interictal stage in a sample of migraine patients without aura are similar to several previous research (8, 11, 14). The rate of perfusion disorder that we found in a significant proportion of patients during the ictal period is consistent with the data from Bednarczyk's study (17) which is important in terms of supporting the idea that migraine with and without aura may be caused by the same disease process.

Our study did not look at the link between pain attacks and changes in brain perfusion over time.

Since the normal group was not formed in our study, a comparison between the patient groups and the normal ones could not be made. However, according to the qualitative evaluation results, it was observed that the mean CCR values of the brain regions considered hypoperfusion in the ictal period were considerably lower than the brain regions considered normal in the ictal period, and this difference was

quite significant in the areas that could be statistically analyzed (superior parietal I and inferior parietal) (p. =0.000, table 4). It was observed that the mean CCR values were close to each other in the brain regions considered qualitatively normal in the ictal and interictal periods, and the difference in 2 of the 17 regions (superior parietal 1 and superior frontal 3) was significant at the $p<0.05$ level. No comparison was made between other data in Table 4 due to the lack of sufficient number of pathological regions. However, it was observed that regions interpreted as hypoperfused in the interictal period had lower CCR values than regions evaluated as normal.

When our study was evaluated in general, it was determined that MwA showed more and significantly decreased cerebral blood flow in interictal and ictal periods than MwoA. It was observed that the hypoperfusion areas observed in MwA affected larger brain regions than in MwoA. Significant differences were detected in 9/17 brain regions between ictal images of patients with and without aura. There were also significant differences in 7/17 regions between interictal images of patients with and without aura. Since interictal SPECT showed reversal of the majority of ictal cCBF changes to normal in MwoA, we think that brain perfusion studies performed only during interictal period will be insufficient to show the changes in CBF in migraine patients especially without aura and this will cause false or negative interpretations.

Extensive data on EEG findings are available in patients with migraine, and the incidence of EEG abnormalities has been published, with rates as high as 70%. However, most EEG findings that are considered normal (posterior slowing, hyperventilation sensitivity, 14-6 Hz positive spike discharges) are found at similar levels in normal controls as well as in migraineurs. The results of D. De Carlo' EEG study (18) on 425 pediatric and adolescent chronic headache patients showed that EEG may show temporary abnormalities, especially in aural migraine patients in the ictal period (focal, hemispheral, or bilateral slowing and continuous beta activity) while it is often normal or may reveal some abnormality without clear clinical relevance during interictal period.

There are some publications showing abnormal EEG findings especially in patients with hemiplegic, basilar and complex neurological aura in the ictal period. Uri Kramer et al (19), in their literature review to investigate the importance of EEG in the evaluation of headache found that mild diffuse slowing of background activity occurs in 3-24% of the EEGs of patients with migraine. In their study, they stated that deceleration was significantly more pronounced in migraine patients than in tension-type headache patients. In the same literature review, it is stated that abnormalities occurring during hyperventilation were recorded in some studies, and it was reported that advanced EEG analyses using differential values (coherence values and alpha values) could distinguish migraine patients from controls. In the interictal and ictal period SPECT and EEG study conducted by S. Soriani et al (4), no abnormality was observed in the EEG recordings made in the interictal period, and only slow-wave activity was observed in 14 out of 19 migraine patients during ictal period.

Quantitative and topographic EEG studies give more accurate results which allow reduced subjectivity. However, we did not perform a quantitative EEG evaluation in our study.

In our study, we found diffuse voltage suppression in ictal period in 3 (33%) of 9 patients with MwA. While this finding was transient in 2 patients, it continued in interictal period in 1 patient. Widespread voltage suppression observed in 3 (27%) of 11 patients with MwoA in the ictal period persisted in 2 of them in the interictal period. Our findings are in agreement with some studies in the literature (18-20). However, the lack of quantitative EEG analysis and lack of diversity in the group of patients, also limited number of cases may have reduced the significance of the results.

There are limited number of studies in the literature in which SPECT and EEG findings are combined in patients with migraine and very few of them have been studied in the childhood age group (3, 4, 8, 9). In the juvenile age group study of Battistella (8) especially in patients with hemiplegic and classical migraine, slow-wave activity in the posterior region was shown consistent with contralateral neurologic symptoms in the ictal period, inconsistent with SPECT findings. In the study of Soriani et al (4) in the juvenile group, it was stated that the side agreement between EEG and brain SPECT asymmetry was high. Mirza et al (9) stated in their study that mild hypoperfusion was observed in patients with interictal EEG abnormalities while Schlake et al (3) revealed EEG findings at certain rates without a definite relationship with the topography of SPECT in adult series of migraine patients with aura. We could not find any study in the literature showing the relationship between SPECT and EEG findings, frequency of attacks, and response to treatment. In our study, we discovered that SPECT and EEG data were not connected to each other or the frequency of attack. Similarly, we found no significant relationship between the length of the patients' therapy and the SPECT and EEG data. However, larger studies with the variety of patients are needed for more significant results.

According to our findings, we think that SPECT can be utilized as an objective diagnostic approach in juvenile patients especially with aural migraine during ictal and interictal phase and in patients with MwoA during ictal phase. Diagnostic yield of EEG is low but could be useful as ictally in certain patients such as hemiplejic and basilar migraine, or as a differential from epilepsia. The presence of cerebral perfusion abnormality in migraine patients who do not have an aura appears to support the theory that both conditions might be due to the same disease mechanism.

Conflict of interest
The authors declared no conflict of interest.

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Authors' contributions
Concept: T.K., Design: T.K., Data Collection or Processing: T.K., M.S., Analysis or Interpretation: A.T.S., M.S., Literature Search: T.K., M.S., S.U., Writing: T.K.

Ethical Statement
Our study has been perfonmed between 1999 and 2000. Since there is no Ethical Committee before 2011, approval has not been taken for this study (no need for approval).

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