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Does migraine affect central auditory processing abilities?

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A R T I C L E I N F O

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A B S T R A C T

Objective: Migraine is a neurological disease associated with an altered cortical excitability level. Several studies have investigated the relationship between migraine and central auditory processing (CAP), with deficits in CAP being common among migraine patients. However, studies on the factors affecting these CAP changes observed in migraine patients are still few and controversial. This study aims to investigate CAP changes in migraine patients with Duration Pattern Test (DPT) and Frequency Pattern Test (FPT), which have not been used in previous studies.
Methods: Sixty subjects were divided into two groups and one migraine subgroup: control group, twenty normal healthy subjects, fourty subjects diagnosed with migraine. They were evaluated using the CAP test including DPT and FPT. To identify the variables and possible effects of the variables, a questionnaire describing the characteristics of migraine features was administered to participants with migraine.
Results: No significant difference was found the between the control and study group in CAP tests scores. No significant correlation was found between migraine characteristics and CAP tests scores. Males had significantly higher FPT scores in both ears than females ($p<0.05$). Significant statistical negative correlation was found between age and FPT scores for both ears and left DPT scores ($p<0.05$).
Conclusion: Although migraine patients generally showed lower CAP ability than the control group, no significant difference was observed between them. This was also valid for subgroups of migraine. However, as age increased in the migraine group, a significant decrease in CAP performance was observed. It was observed that male migraine patients had better CAP ability, especially FPT scores. Migraine may affect performance in CAP depending on gender and age factors.

1. Introduction

Migraine is a common, multifactorial, disabling, recurrent, neurovascular headache disorder that affects more than 10 % of the general population [1]. This disease affects multiple cortical, subcortical, and brainstem areas that regulate autonomic, affective, cognitive, and sensory functions [2,3]. The exact pathophysiological mechanisms underlying migraine-related cognitive symptoms are still unclear, but several hypotheses have been suggested. Researchers attribute migraine-related cognitive symptoms to brain structural anomalies, such as thickening of the somatosensory cortex, and reduced parietal and frontal grey matter [4,5]. The specific cognitive domains involved in migraine-related cognitive impairment are information basic attention, executive functions, verbal and non-verbal memory, and verbal skills related to the activation and integrity of the prefrontal cortex [6].

CAP is the ability of the brain to process and interpret auditory information. CAP includes sound localization and lateralization, auditory discrimination, auditory pattern recognition and temporal aspects of auditory signals (resolution, masking, integration, ordering) [7,8]. The auditory ability to recognize, identify, and sequence sounds involves

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perceptual and cognitive processes [9].

The most common complaint in migraine patients is cognitive problems such as memory and attention, and in studies on this relationship, test methods that evaluate CAP such as Speech in Noise Test, Dichotic Digits Test, Gap in Noise Test, DPT have been used [10]. In addition to these tests, Frequency Pattern Test (FPT) is a frequently used test to perform CAP. FPT and DPT, which are tests that evaluate temporal sequencing skills, provide information about right and left hemisphere function, integration through the corpus callosum, and cognitive and perceptual processes [24]. Studies in patients with central auditory processing disorder (CAPD) have shown that FPT performance is less affected than performance on DPT-like tests, leading to the suggestion that these tests involve different functional processes [11]. The integrity of both brain hemispheres suggests that they are important for the perception and determination of tonal pattern, and FPT assesses the frequency pattern recognition and temporal sequencing task of different stimuli and involves both hemispheres [8,12]. The non-dominance hemisphere (usually the right) is involved in the perception of pitch and recognition of auditory contour, while the dominance hemisphere (usually the left) is important for determining the tone pattern. Assignment of a tonal pattern requires processing of the acoustic boundary that occurs in the right hemisphere and will then be transferred to the left hemisphere via the corpus callosum when the response requires verbalization of the tonal pattern. Thus, when the response to the frequency pattern test requires verbal expression of the tone pattern, the integrity of the right temporal lobe, the corpus callosum tracts, and the left temporal lobe are essential to obtain an adequate response to the test. [13,14]. On the other hand, the DPT detects cortex and inter-hemispheric dysfunctions [15]. The perception of sound stimuli of up to 500 ms involves a basic perceptual sensory mechanism [16]. Approximately 300 ms of sound duration discrimination is mediated by two distinct neural networks: a frontal-parietal area within the cortex and regions encompassing the basal ganglia, cerebellum, and right prefrontal cortex. These latter areas are specifically associated with temporal aspects of sound duration discrimination [17]

It is thought that patients may experience some disorders in auditory processing due to perceptual and cognitive changes in migraine. A limited number of studies have been conducted on this subject and most of the studies showed that CAP disorders are common in migraine patients [18–22]. Tawfik et al. showed that the most frequently affected part of CAP is temporal processing which is 85 % of migraine patients [21]. However, the exact mechanism behind this relationship is not yet well-known. Studies on the factors affecting these CAP changes observed in migraine patients were few and controversial. Some of the studies focused on whether the migraine is with aura (MA) or without aura (MoA). The studies showed that there was no difference for MA and MoA patients in CAP [20]. Tawfik et al. focused on comparing the findings in vestibular migraine vs classic migraine and found worsening of the migraine patients' CAP results but no difference between the groups [21]. Although these studies assess the effects of the duration of illness, frequency, and duration of the attacks, the headache side, data for possible influencing factors were few. They found no correlation between the duration of the disease or the frequency of attacks [21,23].

This study aims to investigate CAP changes in migraine patients with DPT and FPT, which have not been used in previous studies. In addition, we sought to investigate the possible variables expected to cause these changes in migraine subgroups and the effects of these variables.

2. Materials and methods

This study was conducted as a case-control observational study between January and July 2023 and it was approved by the ethical committee of XXX (No: E-10840098–772.02–4593). Participants were informed about the experiment and oral and written consent were obtained from the individuals.

2.1. Subjects

2.1.1. Study group

The study consisted of 40 patients, 15 with MA and 25 with MoA who were diagnosed by XXX Hospital Neurology clinic according to the International Classification of Headache Disorders ICHD-3. Their age ranged from 21 to 50 years.

2.1.2. Exclusion criteria (in both groups)

-Presence of peripheral hearing disorders (>25 dBHL)
-Patients with other types of headaches rather than migraine
-Patients with other neurological disorders
-History of earache, discharge, or surgery
-Physical or emotional disorder that might affect test results

2.1.3. Control group

Consisted of 20 healthy subjects ranging from 21 to 50 years as the control group with the following:

-Bilateral pure tone threshold averages in the normal range (<25 dBHL),
-No history of migraine or other types of headaches,
-No history of other neurological and psychiatric disorders

All participants were matched according to age (mean age of MA=34.2, MoA=30.4 and control group = 27.3) and education (mean years of education in MA=15.2, MoA=14.7 and control group=18.3).

2.1.4. Equipment of experiment

Pure tone audiometry: air conduction (AC) and bone conduction (BC) thresholds for frequencies ranging from 250 to 8000 Hz for AC and from 500 to 4000 Hz for BC (using TDH39 headphones and a Radioear B71 vibrator with a clinical audiometer Interacoustics AC40)

We used the following for the central auditory processing tests;
-A double-walled sound-treated room
-Two-channel audiometer, Interacoustics, model AC40 (Denmark)
-TDH-39 auditory stimulator

We used the following for central auditory processing and neuropsychological tests;
-FPT
-DPT

FPT: This test contains three tones composed of 880 Hz (low) and 1122 Hz (high) frequencies. Each of the tones has 10 ms (ms) rise–fall time and a duration of 200 ms. The interval between the tones within each sequence is 150 ms. This permits the generation of six different sequences of high (H) and low (L) tones: HHL, HLH, HLL, LLH, LHL, and LHH [24]. Individuals were asked to verbally rank the sounds they heard depending to their frequency and order of presentation. Stimuli were presented with insert earphones at 55 dB HL. A total of 60 sets of 30 stimuli for each ear were presented to the individuals, and FPT scores were calculated for both ears separately.

DPT: DPT is applied through three consecutive 1000 Hz tones, one of which is of either longer or shorter duration than the other two. The durations are either 500 ms (long) or 250 ms (short). The intertonal interval is 300 ms, with rise-fall time of 10 ms. Six different sequences of long (L) and short (S) tones are used: LLS, SLL, LSL, SSL, SLS, and LSS [25]. Individuals were asked to verbally rank the sounds they heard depending to their duration and order of presentation. Stimuli were presented with insert earphones at 55 dB HL. A total of 60 sets of 30 stimuli for each ear were presented to the individuals, and DPT scores were calculated for both ears separately.

To identify the variables and possible effects of the variables, a questionnaire describing the characteristics of migraine features was administered to participants with migraine. In this survey; Information were about how long the migraine attack had been present, the frequency and duration of the attacks, the time since the last attack, and its location on the head. It was recorded whether the patient experienced photophobia, phonophobia, nausea, vomiting, tinnitus, movement limitation and imbalance due to migraine.

All tests were carried out by an Audiology Specialist in the Audiology Department of XXX Hospital. All tests were performed with subjects seated in a sound-treated room. All participants received instructions regarding the test performance and practice items prior to the administration of each test.

This manuscript was written in accordance with the Helsinki Declaration. We confirmed a patient's anonymity. We have obtained informed consent from the participant presented in the study.

2.2. Statistical analysis

The Statistical Package for the Social Sciences version 20 (SPSS inc. Chicago, IL, USA) was used for data analysis. The sample size was determined by G*Power (Version 3.1.9.6, Universität Kiel, Germany) analysis. The power analysis revealed a power of 95 % with an effect size of 0.50 (large) at a significance level of 0.05, indicating that a sample size of 34. The normal distribution was evaluated using the Kolmogorov-Smirnov test. Since it was determined that the data did not show a normal distribution, analyses were performed with non-parametric test methods. Thus, spearman correlation analysis was used in the correlation analyses. Mann-Whitney U test was used for pairwise comparison analysis and Kruskal-Wallis test was used for multiple comparison analysis. The level of significance was taken as 0.05.

3. Results

A total of 60 people were included in the study, 20 in the healthy group and 40 in the migraine group. Within the migraine group, 15 patients belonged to MA and 25 patients belonged to the MoA. Demographic data of all participants and data for the migraine groups are shown in Table 1 and Table 2, respectively.

It was observed that the presence of migraine had no effect on CAP scores (Table 3). Despite this, it is thought that possible factors accompanying migraine may have an impact on CAP scores. In addition to aura, which is one of the most frequently researched topics in the evaluation of these factors, it was observed that there was no change in CAP scores when other factors (Table 4), it was observed that there was no change in CAP scores when other factors (onset of migraine, attack frequency and duration, and time since the last attack) were evaluated (Table 5).

The relationship between gender and CAP test scores is shown in Table 6. Males in the migraine group had significantly higher FPT scores in both ears than females ($p<0.05$) and no relationship was found between gender and DPT scores. Although, in the control group, no relationship was found between gender and CAP test scores($p>0.05$), male has still higher results then women.

The correlation between age and CAP test scores was statistically analyzed: a significant negative correlation was found between age and FPT scores for both ears and left DPT scores ($p<0.05$). No significant correlation was found between age and right DPT scores ($p>0.05$). In the control group, no relationship was found between age and CAP test scores ($p>0.05$). Analysis findings are shown in Table 7.

The relationship between the presence of tinnitus and CAP tests scores in migraine group was statistically analyzed. No significant relationship was found ($p>0.05$). The relationship between the side of headache and CAP tests scores in migraine group was statistically

Table 1
Demographic data of both migraine groups and control group.

		Migraine Group (n=40)	Control Group (n=20)	p
Age	**Mean**	31.80	27.45	
	SD	7.80	8.76	0.056
	Range	21–47	19–53	
Gender	**Male**	8 (%20)	9 (%45)	0.067
	Female	32 (%80)	11 (%55)	
Education (years)	**Mean**	14.92	18.35	
	SD	4.34	5.67	0.052

Table 2
Clinical features of migraine patients.

		Migraine with Aura (n=15)	Migraine without Aura (n=25)	p
Onset of migraine (years-old)	**Mean**	9.40	7.84	0.462
	SD	5.77	7.35	
Attack frequency (per month)	**Mean**	4.20	4.24	0.969
	SD	2.83	3.51	
Time elapsed since last attack (day)	**Mean**	31.06	14.72	0.062
	SD	39.48	12.93	
Attack duration (hour)	**Mean**	13.66	19.36	0.298
	SD	14.48	19.39	
Tinnitus	**Yes**	6 (%40)	8 (%32)	0.736
	No	9 (%60)	17 (%68)	
Side of headache	**Right**	1 (%6.70)	4 (%16)	
	Left	3 (%20)	6 (%24)	0.614
	Non-specific	11 (%73.30)	15 (%60)	
Phonophobia	**Yes**	10 (%66.70)	21 (%84)	0.255
	No	5 (%33.30)	4 (%16)	
Photophobia	**Yes**	11 (%73.30)	23 (%92)	0.174
	No	4 (%26.70)	2 (%8)	

Table 3
Investigation of the relationship between the presence of migraine and CAP test scores.

	Control Group (n=20)		Migraine Group (n=40)		p
	Mean	**SD**	**Mean**	**SD**	
FPT % (R)	72.22	14.16	60.93	24.66	0.120
FPT % (L)	67.08	16.43	65.50	21.57	0.775
DPT % (R)	84.62	13.06	79.30	20.30	0.582
DPT % (L)	83.62	13.19	81.18	17.62	0.814

Table 4
Investigation of the relationship between the presence of aura and CAP test scores.

	Migraine with Aura (n=15)		Migraine without Aura (n=25)		p
–	**Mean**	**SD**	**Mean**	**SD**	
FPT % (R)	59.66	18.24	61.70	28.16	0.761
FPT % (L)	63.50	21.39	66.70	22.02	0.761
DPT % (R)	80.66	21.84	78.48	19.73	0.525
DPT % (L)	80.66	20.84	81.50	15.84	0.804

Table 5
Investigation of the relationship between migraine characteristics and CAP tests scores.

		Onset of migraine (years-old)	Attack frequency (per month)	Attack duration (hour)	Time elapsed since last attack (day)
FPT % (R)	**r**	0,019	0,022	0,122	0,017
	p	0,906	0,892	0,453	0,919
FPT % (L)	**r**	-0,165	-0,035	0,050	0,084
	p	0,309	0,832	0,760	0,605
DPT % (R)	**r**	-0,106	-0,061	0,086	0,143
	p	0,516	0,709	0,599	0,380
DPT % (L)	**r**	-0,136	-0,008	0,028	0,070
	p	0,403	0,962	0,865	0,670

Table 6
Comparison of CAP test scores across gender in migraine and control group.

Groups	Gender	FPT-R (%)		FPT-L (%)		DPT-R (%)		DPT-L (%)	
		Mean ± SD	p	Mean ± SD	p	Mean ± SD	p	Mean ± SD	p
Migraine Group	F	55.15±22.26	0.001*	60.46±20.05	0.002*	76.78±21.69	0.209	79.14±18.80	0.153
	M	84.06±20.78		85.62±15.28		89.37±8.10		89.37±8.31	
Control Group	F	68.33±14.84	0.297	64.75±16.60	0.460	83.18±14.96	0.710	82.95±14.48	0.941
	M	76.11±13.11		70.00±16.85		86.38±10.90		84.44±12.23	

(F: Female, M: Male)

Table 7
Correlation analyses between age and CAP test scores in migraine group.

Migraine group		FPT % (R)	FPT % (L)	DPT % (R)	DPT % (L)
Age	r	-0,326	-0,318	-0,205	-0,322
	p	0,040*	0,045*	0,204	0,043*
Control group		**FPT % (R)**	**FPT % (L)**	**DPT % (R)**	**DPT % (L)**
Age	r	-0,200	-0,163	0,073	-0,127
	p	0,398	0,493	0,760	0,594

analyzed. No significant relationship was found (p>0.05).

4. Discussion

Migraine is a neurological disease associated with an altered cortical excitability level [26]. Several studies have investigated the relationship between migraine and CAP, with deficits in auditory processing being common among migraine patients [27,28]. However, studies on the factors affecting these CAP changes observed in migraine patients are still few and controversial. The current study showed that migraine disease may lead to poor performance on CAP tests in some parameters. [27,28]

Female patients participated more in present study. This agreed with the data reported by previous studies [10,31,32]. Moreover, we found no significant difference in education level between the control and study groups (Table 1). Studies have reported that the prevalence of migraine is found at the middle education level (33). Also, it has been mentioned that as the educational level decreases, the prevalence of migraine increases at low social class and education level due to more exposure to sunlight, brightness and extreme air temperature due to work conditions and working in occupations with physical stress [34, 35]. Yeral and Serbetcioglu did not find any relationship between gender and CAP in individuals with normal hearing evaluated by FPT and DPT [29]. Our findings agreed with that study for control group. However, the FPT scores of males in the migraine group were significantly higher compared to females (Table 6). Furthermore, the FPT and DPT scores of females with migraine were lower compared to the control group, it was the vice versa in males with migraine. Although we could not explain the exact reason for these findings, possible reasons include the low number of participants and more frequent and severe attacks in females.

Researchers evaluating CAP and its relationship with memory and attention in migraine patients, such as Speech Intelligibility in Noise Test, Dichotic Digit Test, Gap in Noise Test and DPT, poor performance was found in the migraine group, but no distinction was evaluated between migraine with and without aura patients [21]. Present study, the correct answer percentages from FPT tests evaluated together with DPT did not show a significant difference between migraine and control groups and between migraine subgroups (Table 3 and Table 4). Contrary to previous findings reported by other researchers, in this study, it was not observed that the auditory ability of temporal ordering and the physiological mechanism of temporal processing assessed by DPT were affected in migraine patients. Also, it was found that the frequency pattern recognition and tonal pattern perception performances of different stimuli were not affected by the FPT test, which was not evaluated in other studies.

Yeral and Serbetcioglu did not find any relationship between age and CAP in individuals with normal hearing aged between 20 and 40 years [29]. Our findings coincide with Yeral and Serbetcioglu for the control group. However, in the migraine group, we found a negative correlation between age and FPT scores for both ears and left DPT scores (Table 7) (Figs. 1 and 2). It is known that CAP skills decrease with age [30]. In contrast to the control group, we thought that the decrease in CAP skills with age in the migraine group may be related to migraine characteristics such as attack frequency and attack duration. However, we did not find any relationship between migraine characteristics and CAP skills (Table 5). Considering these findings, it may be concluded that the effect of age on the central nervous system is more prominent in the migraine group compared to the control group.

In the literature, there are contradictory results in studies examining the relationship between the presence/absence of aura and cognitive and CAP skills. Wen et al. found that migraine patients with aura exhibited better cognitive skills compared to those without aura [31]. On the other hand, Agessi et al. found no significant difference between MA and MoA in terms of CAP [20]. We did not find a correlation between the presence/absence of aura and CAP skills in agreement with Agessi et al. In addition, since we did not observe any difference for CAP test scores between MA with and MoA, we compared the sum of both groups with the control group. We did not find any difference between the migraine group and the control group in terms of CAP (Table 3). Considering the relationship between CAP skills and cognitive functions, it is thought that this situation creates a contradiction. The mechanism underlying the cognitive difference between the two groups may be different from the mechanisms involved in CAP tests. In addition, we thought that this difference may be due to methodological differences (assessment methods) in the studies aforementioned.

Tawfik showed that there was no statistically significant relationship between the number of attacks and disease duration in migraine patients and CAP results [10]. Supporting this idea, present study, no significance was found between CAP scores and migraine characteristics such as onset of migraine, time elapsed since last attack, attack frequency and duration (Table 5). A different study on cortical event-related potentials noted that there was no significant correlation between the parameters and disease duration, supporting the recent theory that migraine occurs not due to repeated ischemia caused by repeated attacks, but due to the release of neurogenic inflammation [32].

Tinnitus and migraine can occur together, and people with tinnitus may report migraine and other headache disorders. One the one hand, previous studies stated that there is a relationship between tinnitus and migraine [33,34], on the other hand a different study showed that this relationship was not a meaningful association [35]. However, such studies have not focused on the subgroups of migraine and its relationship with CAP. Present study, in which we observed that tinnitus complaints were less in migraine patients, revealed that there was no significant difference in the presence of tinnitus between migraine subgroups in CAP tests.

When the nature of the headache is examined in studies, it is stated that the pain is unilateral and throbbing in most patients [10,36]. In our study, no significant difference was found when CAP scores were evaluated according to pain localization in the migraine group. In addition,

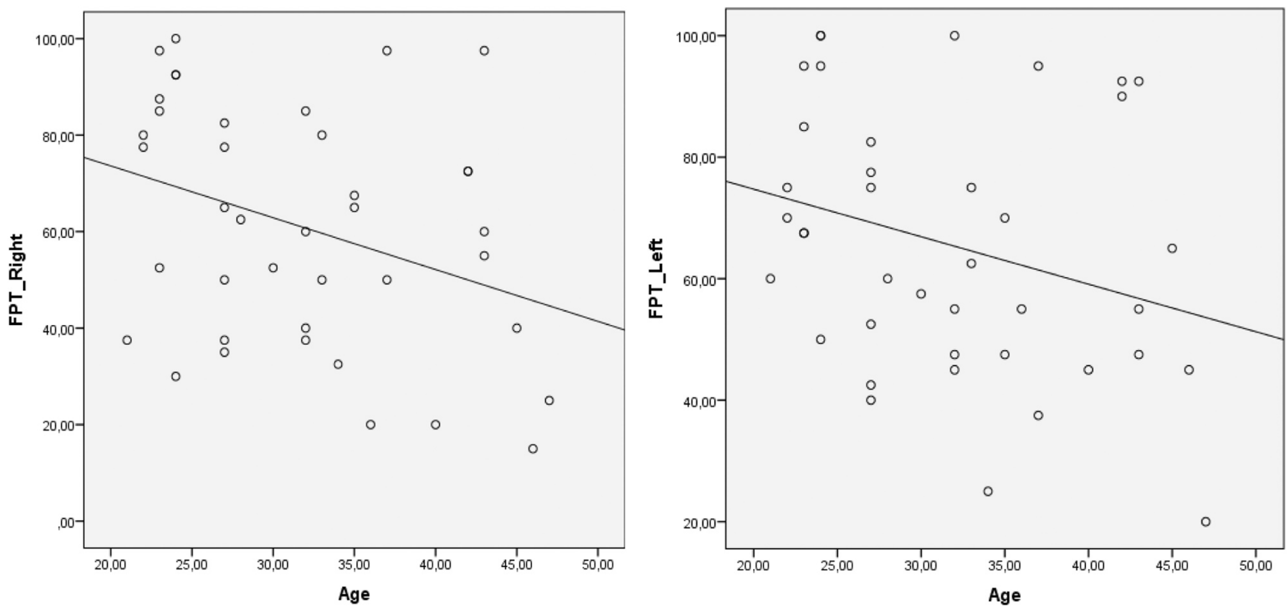

Fig. 1. Scatter graphs of the correlation between age and FPT scores in both ears.

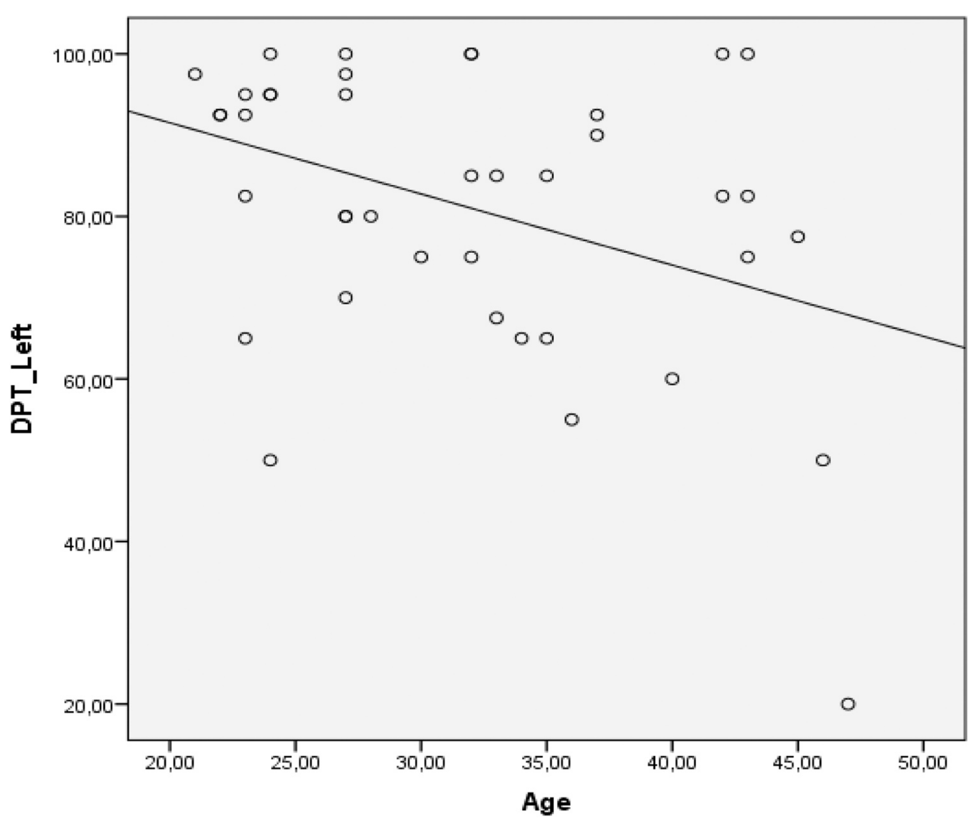

Fig. 2. Scatter graph of the correlation between age and DPT scores in left ear.

although no significant difference was found in this study, it was observed that the MoA group complained more about phonophobia. It has been reported that the most common auditory symptoms in migraine are phonophobia [37] and that the complaint of phonophobia accompanies photophobia in patients [38–40]. In our study, it was observed that phonophobia complaints were more common in the MoA group than in the MA group, but this did not show a significant difference (Table 2). Accordingly, these similarities between phonophobia and photophobia in migraine provide evidence to other studies that both phenomena share a common pathophysiological mechanism.

5. Conclusion

Considering FPT scores, male migraine patients were found to have better CAP ability compared to females. Furthermore, a negative correlation was found between age and FPT and DPT scores. These findings showed that gender and age are important variables in migraine-related CAP impairment. Based on these findings, it can be concluded that early auditory rehabilitation interventions may contribute to a favorable prognosis for CAP in these individuals. We found that migraine characteristics and migraine subgroups (MoA and MA) had limited effects on CAP. There was no difference in CAP skills between migraine and control groups. These findings should be addressed in further studies with cognitive assessments and larger sample sizes.

6. Limitations and future research

We evaluated the CAP only with FPT and DPT, which assess temporal sequencing ability. In future research, the role of gender and age in the association between migraine and CAP can be evaluated with a larger population especially for more robust correlation analysis and a more comprehensive CAP test battery (Temporal Gap Detection, Dichotic Digit, etc.).

Disclosure statement

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CRediT authorship contribution statement

Oguz Yilmaz: Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Burcu Polat:** Writing – review & editing, Supervision, Resources, Methodology, Data curation, Conceptualization. **Ogulcan Gundogdu:** Writing – original draft, Methodology, Data curation, Conceptualization. **Handan Yaman:** Writing – review & editing, Writing – original draft, Validation, Resources, Methodology, Investigation, Data curation, Conceptualization. **Cem Yeral:** Writing – review & editing, Writing – original draft, Validation, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Berna Ozge Mutlu:** Writing – original draft, Methodology, Investigation, Data curation, Conceptualization.

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