



Evaluating the Relationship Between Migraine and Cognitive Function by Using the Frontal Assessment Battery (FAB)

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Abstract

Background: Migraine is recognized as one of the most prevalent disorders worldwide. Previous imaging studies suggest some structural changes in the brains of migraine patients. Studies investigating the relationship between migraine and cognition have shown conflicting results.

Objectives: The present study aims to evaluate the association between migraine and cognitive function using the frontal assessment battery (FAB) test.

Methods: In this prospective cross-sectional study, 96 participants, including 48 migraine patients and 48 healthy subjects, were recruited. Migraine was diagnosed and classified as migraine without aura (MO) and migraine with aura (MA), based on the international classification of headache disorders, third edition (ICHD-3). All participants were interviewed, and demographic and migraine-specific variables (duration of the disease, frequency of the disease, severity of headaches, preventive medication use) were collected. Cognitive function was then assessed using the FAB, a validated tool for assessing frontal lobe cognitive functions.

Results: Of the 48 migraine patients, 10 were diagnosed with MA, and 38 were diagnosed with MO. The FAB results were significantly lower in migraine patients compared to controls (median \pm [interquartile range (IQR)]: 15.00 [4.00] vs. 16.00 [3.75], P -value = 0.04). Furthermore, patients with MO (14.00 [5.00]) had significantly lower FAB scores than the control group (P -value = 0.01). No significant differences were observed between patients with MA and either the control group (15.50 [1.50], P -value = 0.82) or MO patients (P -value = 0.09). Additionally, a moderate positive correlation between FAB scores and years of education (r = 0.54, P -value < 0.001) and mild negative correlations with age (r = -0.32, P -value < 0.001) and Body Mass Index (BMI) (r = -0.35, P -value < 0.001) were observed. No significant associations were found between FAB scores and sex, smoking, drinking, or migraine-specific variables.

Conclusions: The present study suggests that a history of migraine, especially MO, could worsen cognitive function. However, we cannot specify the relationship between MA and cognition, nor its differences with MO. Additionally cognition could have a moderate positive correlation with years of education and a mild negative correlation with age and BMI. Moreover, disease duration, frequency, severity, or preventive medication use did not have a significant impact on cognitive performance in migraine patients.

Keywords: Aura, Cognition, Education, Frontal Lobe, FAB, Migraine

1. Background

Migraine is a headache disorder considered among the top 10 specific causes of disability and is the third most prevalent disorder worldwide, affecting 14.7% of

the global population (1, 2). In a study conducted in the USA among 162,576 participants, the prevalence of migraine was found to be 11.7%, with a higher prevalence in participants aged 30 - 39 years (3). Additionally, it has been reported that migraine is most common among Caucasians (4) and has an estimated annual cost of 9.2 billion dollars (5).

Migraine, as a chronic neurological disorder, is characterized by a unilateral, paroxysmal, pulsating headache with attacks lasting between 4 - 72 hours, usually accompanied by nausea, phonophobia, and photophobia. Migraine includes two major subtypes: (1) Migraine without aura (MO) and (2) Migraine with aura (MA), which constitutes about 30% of migraineurs. It should be noted that the exact pathological and neurological etiology of migraine remains controversial (1).

Numerous imaging studies on the brains of migraine patients suggest some structural changes compared to healthy populations (6-12). For instance, in a cross-sectional study of structural brain lesions and headaches in 780 elderly participants, Kurth et al. demonstrated that any history of chronic severe headaches was correlated with higher risks of increased volumes of white matter hyperintensity (6). In another study, Mathur et al. showed that migraine could reduce neural activities associated with cognition in brain regions related to cognitive processing (7). In a paper exploring migraine, cognition, and brain structure, Nichole Schmitz et al. reported decreased parietal and frontal lobe gray matter density in migraineurs compared to the healthy/control group. They also highlighted a significant correlation between delayed response time and reduced frontal lobe gray matter density, suggesting the possible effect of migraine on the cognitive functions of the frontal lobe (8).

According to these structural changes in the brains of migraine patients, brain functions, particularly cognitive functions, should be assessed. Studies investigating the relationship between migraine and cognition have shown conflicting results. Some studies suggest that migraine could lead to poorer cognitive functions (13-16). Conversely, other studies suggest that migraine does not affect cognition (17-19). However, some studies indicate that migraine may enhance cognitive functions (20, 21).

Additionally, some of these studies also present discrepant results regarding the effects of MA and MO

on cognitive function (13, 15, 16, 18, 20, 21). De Araujo et al. suggested more adverse changes in cognition in patients with MA (15), whereas Pellegrino Baena et al. suggested that MO, but not MA, could worsen cognition (16). Interestingly, some studies show better cognitive function in patients with MA or MO compared to healthy subjects (20, 21). Given that the frontal lobe plays an integral role in cognition (22) and its migraine-induced structural changes observed in previous imaging studies (8, 11), the relationship between migraine and the cognitive functions of the frontal lobe should be assessed. A simple tool to evaluate the cognitive function of the frontal lobe is the frontal assessment battery (FAB) test (23), a bedside test designed to assess frontal lobe functions and dysexecutive syndrome. The overall score of the FAB can determine the severity of the dysexecutive syndrome and might evaluate executive dysfunction (23).

The FAB has been demonstrated as a reliable instrument for detecting cognitive impairment in diseases such as amyotrophic lateral sclerosis (ALS), dementia, and Parkinson's disease (PD) (24-27). Interestingly, Terada et al. suggested that in Alzheimer's disease (AD) patients, the results of the FAB are more correlated with neurodegenerative changes seen in the frontal lobe than with amyloid-beta ($A\beta$) deposition and pathology (28). Furthermore, the FAB is suggested to be a determining tool for detecting frontal lobe lesions in disorders such as frontal lobe tumors and frontal cortex stroke (29, 30).

Studies that have evaluated cognition using the FAB in migraine patients are limited. Deodato et al. observed that the FAB results showed a notable reduction in patients with MO compared to healthy controls (31). Additionally, Le Pira et al., by comparing the FAB results in patients with MA and the control group, observed a considerable decline in FAB scores in patients with MA (13).

2. Objectives

Given the conflicting results in previous studies regarding the relationship between migraine and cognition, as mentioned above, and the abnormal structural findings in previous imaging studies found in the brains of migraineurs, particularly in their frontal lobe (6-12), the relationship between migraine and cognition should be assessed from different perspectives and cognitive tests. This approach will lead

to a better understanding of the cognitive effects of migraine. Considering the limited number of studies using the FAB to evaluate cognitive functions in migraineurs and the discrepant findings on the effects of MA and MO on cognition, the present study employs the FAB test to evaluate the association between migraine and cognitive function, especially in the frontal lobe.

3. Methods

3.1. Study Design, Setting, and Participants

This prospective cross-sectional study included 48 migraine patients and 48 healthy subjects. The study was conducted in accordance with the STROBE guidelines, based on data collected between June and November 2022 in the neurology department of Tehran Imam Khomeini Hospital clinics (Appendix 1 in Supplementary File).

Migraine patients were initially selected through consecutive sampling from those referred to the clinic. All included migraine patients were over 18 years of age, had not experienced any headaches 25 hours prior to the interview, and were diagnosed based on the international classification of headache disorders, 3rd edition (beta version) (ICHD-3 beta) criteria. Migraine patients with any history of central or peripheral nervous system disorders, diagnosed psychological disorders based on clinical or medical records, or use of narcotics or hallucinogenic drugs were excluded.

Control subjects were gathered using frequency and stratified matching methods to ensure comparability across potential confounding variables such as age, sex, years of education, Body Mass Index (BMI), smoking status, and drinking history. All control subjects were healthy individuals over 18 years of age, chosen from patients' families and healthcare workers. Those with any history of prior migraine diagnosis, moderate to severe headaches, frequent headaches, central or peripheral nervous system disorders, diagnosed psychological disorders based on clinical or medical records, or use of narcotics or hallucinogenic drugs were excluded. All participants in this study were native Farsi speakers.

3.2. Ethical Considerations

This project was approved by the ethics committee of the Tehran University of Medical Sciences and was found

to be in accordance with the ethical principles and the national norms and standards for conducting medical research in Iran (approval ID: [IR.TUMS.IKHC.REC.1401.142](#)). All participants provided informed verbal and written consent.

3.3. Covariates and Measurements

This study evaluated the FAB results of the study groups and independent variables. These variables consist of two groups:

3.3.1. Demographic Variables (Non-migraine-Specific Variables)

- (1) Sex: Male or female
- (2) Age: Years
- (3) Smoking: A positive history was defined as at least one year of continuous smoking during their life (32) or a history of smoking for at least one month in the previous year of the interview (33).
- (4) Drinking: History of consuming alcohol every week.
- (5) Education: Total years of education of each participant.
- (6) The BMI: Calculated based on standard criteria (34).

3.3.2. Migraine-Specific Variables

- (1) Duration of the disease: The period between the diagnosis of the disease and our interview.
- (2) Frequency of the disease: Number of days in a month during which participants had headaches.
- (3) Severity of headaches: Evaluated based on a self-reported numerical pain rating score (35) between 0 (no pain) and 10 (worst imaginable pain).
- (4) History of any preventive drug usage.

Frequency and stratified matching methods were applied to select the control group based on the demographic variables mentioned above to control the potential confounding effect of these variables. To further assess the potential confounding effect, demographic variables were compared between the migraineurs and the control group using statistical tests to confirm that there were no significant differences between these two groups.

In this study, the primary outcome was the comparison of the FAB results between all migraine

patients and the control group, as well as the comparison of the FAB results based on demographic and migraine-specific variables (as mentioned above). However, some studies comparing cognition levels between patients with MA, MO, and healthy subjects have reported discrepant results, as mentioned earlier (13, 15, 16, 18, 20, 21). Therefore, we decided to add an alternative (accessory) objective, in which patients with MA, MO, and the control group were compared and analyzed for demographic variables and the FAB results. MA and MO were diagnosed based on ICHD-3 beta.

3.4. The Frontal Assessment Battery

The FAB is a scoring test with a maximum score of 18 and a minimum score of 0, designed to evaluate frontal lobe dysfunction. It is divided into six subsets based on six different frontal lobe cognitive functions: (1) Conceptualization, (2) mental flexibility, (3) motor programming, (4) sensitivity to interference, (5) inhibitory control, and (6) environmental autonomy. Each subset is scored from 0 to 3 based on its criteria. The test has demonstrated good interrater reliability ($k = 0.87$, $P < 0.001$), internal consistency (Cronbach's coefficient alpha was 0.78%), and discriminant validity, with 89.1% of cases correctly identified in discriminant analysis of patients and controls (23).

The Persian-translated version of the FAB test has been validated in healthy individuals and patients with Parkinson's disease, demonstrating its reliability as a tool for assessing frontal lobe functions and its utility in evaluating cognitive decline and executive functions in the Iranian population (24). Following a thorough history taking, a general practitioner, trained by a neurologist in the standardized administration and scoring of the Persian-translated FAB test, administered the Persian-translated version of the FAB test during participants' clinic visits.

3.5. Sample Size Calculation and Power Analysis

The G*Power software was utilized to perform the sample size calculation. Based on previous research, the effect size (Cohen's d) was set at 0.58, which represents a moderate-to-large effect (14). Furthermore, the significance level (α) and statistical power ($1-\beta$) were set at 0.05 and 80%, respectively. Additionally, an equal allocation ratio (1:1) was used. This analysis indicated that a minimum of 96 participants (48 per group) were needed.

3.6. Statistical Analysis

This study used SPSS version 18 (Armonk, NY: IBM Corp) to perform the statistical analyses. The Kolmogorov-Smirnov z-test was used to assess the normal distribution of quantitative variables. After matching, statistical tests were performed to ensure that there were no significant differences between the migraine and control groups for demographic variables. Categorical variables such as sex, smoking, and drinking status were compared using the chi-squared test, while continuous variables such as age, BMI, and years of education were compared using the Mann-Whitney U test.

The statistical tests used for investigating the relationship between variables are as follows: The Spearman rank-order correlation coefficient was utilized for comparing quantitative variables where the data did not have a normal distribution. The Mann-Whitney U test and Kruskal-Wallis test were used for comparing qualitative variables with quantitative variables with non-normally distributed data. For categorical data, the chi-squared test was utilized for the comparison of qualitative variables. The results are presented as follows: For quantitative variables, we used mean \pm standard deviation (STD), and median [interquartile range (IQR)] and for qualitative variables frequency (percentage) were used. All reported probability values were two-tailed, and a P-value < 0.05 was considered statistically significant.

4. Results

Of the 96 participants included in this cross-sectional study, 48 were healthy subjects (11 males, 37 females) with a median age of 40.50 years and an IQR of [18.75]. The remaining 48 were migraine patients (9 males, 39 females) with a median [IQR] age of 38.00 [13.00], of which 10 were diagnosed with MA and 38 with MO. The median [IQR] years of education for all participants, the control group, and all migraine patients were 16.00 [6.00], 16.00 [6.00], and 13.50 [4.75] years, respectively. Except for age, there were no significant differences between any of the non-migraine-specific variables (P -value > 0.05). Additionally, there were no significant differences in age between the control group and all migraine patients, nor between the control group and patients with MO (P -value > 0.05). However, there was a significant difference in age between the control group

Table 1. All Subjects' Characteristics ^a

Variables	All Participants (N = 96)	Control (N = 48)	Migraine (N = 48)	MO (N = 38)	MA (N = 10)	P-Value Between Migraine and Control Group	P-Value Between Control, Migraine with and Without Aura
Sex						0.61 ^b	0.876 ^b
Female	76 (79.2)	37 (77.1)	39 (81.3)	31 (81.6)	8 (80.0)		
Male	20 (20.8)	11 (22.9)	9 (18.8)	7 (18.4)	2 (20.0)		
Age						0.30 ^c	0.01 ^{d,e}
Mean ± STD	39.55 ± 11.51	41.02 ± 12.04	38.08 ± 10.88	40.36 ± 10.43	29.40 ± 8.07		
Median [IQR]	40.00 [15.75]	40.50 [18.75]	38.00 [13.00]	40.50 [10.00]	27.50 [14.00]		
Education						0.40 ^c	0.32 ^c
Mean ± STD	14.07 ± 4.48	14.37 ± 4.28	13.77 ± 4.71	13.28 ± 4.74	15.60 ± 4.32		
Median [IQR]	16.00 [6.00]	16.00 [6.00]	13.50 [4.75]	12.00 [4.00]	16.00 [6.00]		
BMI						0.40 ^c	0.59 ^e
Mean ± STD	25.60 ± 4.82	26.15 ± 5.50	25.06 ± 4.02	25.28 ± 4.35	24.21 ± 2.34		
Median [IQR]	24.92 [5.18]	25.47 [6.11]	24.68 [4.57]	24.88 [5.47]	24.50 [2.82]		
Alcohol						0.18 ^b	0.09 ^b
Non-drinker	86 (89.6)	45 (93.8)	41 (85.4)	31 (81.6)	10 (100.0)		
Drinker	10 (10.4)	3 (6.3)	7 (14.6)	7 (18.4)	0 (0.0)		
Smoking						1.00 ^b	0.28 ^b
Non-smoker	80 (83.3)	40 (83.3)	40 (83.3)	30 (78.9)	10 (100.0)		
Smoker	16 (16.7)	8 (16.7)	8 (16.7)	8 (21.1)	0 (0.0)		

Abbreviations: MO, migraine without aura; MA, migraine with aura; STD, standard deviation; IQR, interquartile range; BMI, Body Mass Index.

^a Values are expressed as No. (%) unless otherwise indicated.

^b Chi-square test.

^c Mann-Whitney test.

^d Statistically significant.

^e Kruskal-Wallis test.

and patients with MA (P-value < 0.001), as well as between patients with Migraine with Aura and those with MO (P-value < 0.001). Other demographic and clinical characteristics of all participants are shown in [Table 1](#).

All quantitative variables, including the FAB results, age, education, and BMI, were distributed non-normally. The FAB results in all migraine patients (median [IQR] FAB score: 15.00 [4.00]) were significantly worse than those in the control group (median [IQR] FAB score: 16.00 [3.75]) (P-value = 0.04). Moreover, the performance of patients with MO (median [IQR] FAB score: 14.00 [5.00]) in the FAB results was significantly lower than that of the control group (P-value = 0.01). However, the differences in the FAB results between patients with MA (median [IQR] FAB score: 15.50 [1.50]) and the control

group (P-value = 0.82), as well as between patients with MA and MO (P-value = 0.09), were not of significant importance ([Table 2](#)).

Regarding the numerical variables, there was a moderate statistically significant positive correlation between the FAB results and years of education (correlation coefficient = 0.54, R² linear = 0.395, P-value < 0.001) and a mild statistically significant negative correlation between the FAB results and age (correlation coefficient = -0.32, R² linear = 0.149, P-value < 0.001) and BMI (correlation coefficient = -0.35, R² linear = 0.152, P-value < 0.001) ([Figure 1](#)).

As for qualitative variables, the differences in FAB results between males (median [IQR] FAB score: 15.00 [3.50]) and females (median [IQR] FAB score: 15.00

Table 2. Frontal Assessment Battery Results Between Study Groups ^a

Variables	Total	FAB	FAB	P-Value ^b
All participants	96 (100)	14.43 ± 2.94	15.00 [4.00]	
Groups between all participants				0.04 ^c
Control/healthy	48 (50)	14.95 ± 2.79	16.00 [3.75]	
All migraine patients	48 (50)	13.91 ± 3.03	15.00 [4.00]	
Groups between all participants				0.03 ^d
Control/healthy	48 (50)	14.95 ± 2.79	16.00 [3.75]	
MO	38 (39.6)	13.50 ± 3.21	14.00 [5.00]	
MA	10 (10.4)	15.50 ± 1.43	15.50 [1.50]	

Abbreviations: FAB, frontal assessment battery; STD, standard deviation; IQR, interquartile range.

^a Values are expressed as No. (%) or mean ± STD or (median [IQR]).

^b Statistically significant.

^c Mann-Whitney test.

^d Kruskal-Wallis test.

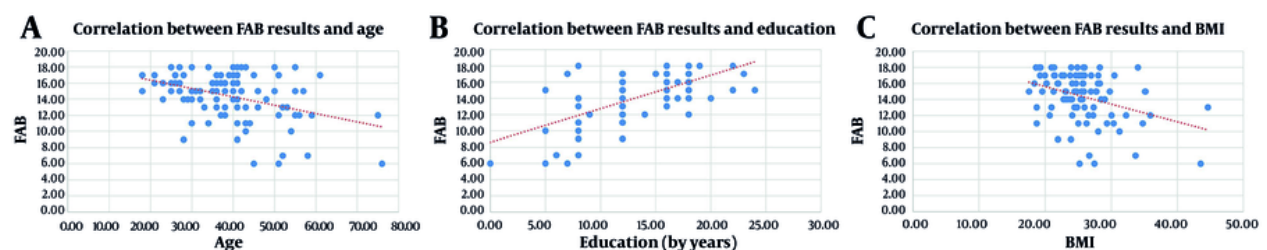


Figure 1. Scatter plots showing the correlation between frontal assessment battery (FAB) results and age (A), education (B), and Body Mass Index (BMI) (C). The BMI, with trendlines. A positive moderate correlation was observed between FAB results and education (correlation coefficient = 0.54, P-value < 0.001), while negative mild correlations were found with age (correlation coefficient = -0.32, P-value < 0.001) and Body Mass Index (BMI) (correlation coefficient = -0.35, P-value < 0.001).

[4.00]) were not statistically significant (P-value = 0.87). Regarding drinking, there were no significant differences in FAB results between drinkers (median [IQR] FAB score: 15.50 [3.75]) and non-drinkers (median [IQR] FAB score: 15.00 [4.00]) (P-value = 0.49). Furthermore, smokers with a median [IQR] FAB score of 15.00 [3.00] showed no significant differences compared to non-smokers (median [IQR] FAB score: 15.00 [4.00]) (P-value = 0.64) (Figure 2).

Additionally, there were no significant differences in the FAB results based on preventive drug usage and the duration, frequency, and severity of the disease. The FAB results based on each migraine-specific variable are shown in Table 3.

5. Discussion

This study aimed to evaluate the relationship between migraine and cognition using the FAB test. In the present study, the FAB results in all migraine patients were significantly worse than those in the control group. Additionally, the performance of patients with MO in the FAB results was considerably lower than that of the control group, suggesting worse cognitive function in all migraine patients, and specifically in patients with MO, compared to the control group. However, the differences in the FAB results between patients with MA and the control group were not significantly important. Also, in our study, the FAB results in patients with MA were higher than in patients with MO, but these results were not considerably important.

The differences in age between patients with MA and MO, and between patients with MA and healthy subjects,

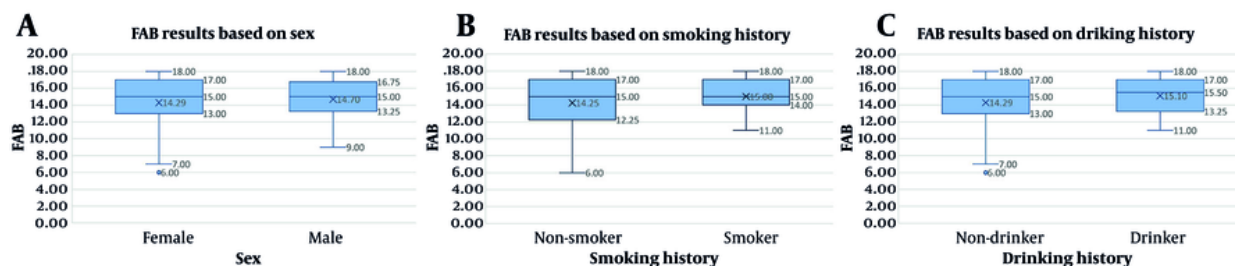


Figure 2. Box plots comparing frontal assessment battery (FAB) results based on sex (A), smoking history (B), and drinking history (C). Median FAB scores did not significantly differ between males and females (P-value = 0.87), smokers and non-smokers (P-value = 0.64), or drinkers and non-drinkers (P-value = 0.49).

Table 3. Frontal Assessment Battery Results Based on Migraine-Specified Variables ^a

Variables	Migraine Patients (N = 48)	FAB	FAB	P-Value Between All Migraine Patients
Duration of disease (y)				0.64 ^b
Under 1	13 (27.1)	14.23 ± 2.71	15.00 [4.50]	
1 to 5	16 (33.3)	14.31 ± 3.23	15.00 [3.75]	
5 to 10	8 (16.7)	12.75 ± 3.61	13.00 [4.00]	
More than 10	11 (22.9)	13.81 ± 2.82	15.00 [3.00]	
Days of headaches in a month (d)				0.52 ^b
1 - 10	29 (60.4)	13.96 ± 3.71	15.00 [6.00]	
11 - 20	11 (22.9)	13.81 ± 1.88	14.00 [3.00]	
21 - 30	8 (16.7)	13.87 ± 1.12	14.00 [2.00]	
Severity of headaches				0.97 ^b
Mild (1 - 3 scores)	4 (8.3)	14.00 ± 4.24	14.50 [8.00]	
Moderate (4 - 6 scores)	13 (27.1)	13.15 ± 4.33	15.00 [7.50]	
Severe (7 - 10 scores)	31 (64.6)	14.22 ± 2.17	14.00 [3.00]	
Preventive medication use				0.73 ^c
Using treatment	32 (66.7)	13.90 ± 3.31	15.00 [4.00]	
Not using treatment	16 (33.3)	13.93 ± 2.46	14.00 [4.00]	

Abbreviations: FAB, frontal assessment battery; STD, standard deviation; IQR, interquartile range.

^a Values are expressed as No. (%) or mean ± STD or (median [IQR]).

^b Kruskal-Wallis test

^c Mann-Whitney test

were significant. Thus, age could be considered a confounding factor in our study. However, the differences in age between all migraine patients and healthy subjects, and between patients with MO and healthy subjects, were not statistically significant. Therefore, the comparison of FAB results between patients with migraine and healthy subjects was not affected, and age had no confounding effect on our primary objective. Furthermore, it should be mentioned

that age only had a weak negative correlation with the FAB results (Figure 1).

Studies investigating the relationship between migraine and cognition have shown conflicting results. Some studies suggest that migraine could lead to poorer cognitive functions. For instance, in a survey of 44 migraine patients and 16 control subjects, it was demonstrated that migraineurs generally had inferior results in cognitive tests; also, patients with MA performed worse in the FAB than patients with MO (13).

In a meta-analysis of 17 studies on migraine and cognitive deficits, Braganza et al. suggested that migraine could have a negative, moderate effect on spatial cognition, executive function, immediate and delayed memory, and complex attention (14). Furthermore, de Araujo et al., in a systematic review of 23 studies on cognition, migraine, and cognitive impairment, proposed that migraine might increase the risk of cognitive impairment, with patients with MA displaying more cognitive changes (15). Additionally, Pellegrino Baena et al., in a cross-sectional analysis of the association between cognitive function and migraine among 4208 participants of the Brazilian Longitudinal Study of Adult Health, ELSA-Brasil, observed that migraineurs in general and patients with MO had poorer performance in cognitive tests; however, these results were not observed in patients with MA (16).

On the other hand, some studies suggest that migraine does not affect cognition. In a prospective cohort study, Rist et al. found that among 1170 participants (167 had migraine) of the epidemiology of vascular ageing study, using nine different tests, including the mini-mental state examination (MMSE), there was no greater cognitive decline in migraine patients compared to healthy participants (17). Also, in a blinded study on four different cognitive tests, Pearson et al. found that patients with both MA and MO did not differ significantly from matched controls (18).

However, other studies suggest that migraines may enhance cognitive functions. In a survey of 21 patients with MO and 21 healthy participants, Baschi et al. observed that MO was associated with better performances in learning and visuospatial memory (20). In a cross-sectional analysis of 6708 participants of the Rotterdam study, Wen et al. showed that patients with migraine, and especially those with MA, had better results in the MMSE, letter-digit substitution test, 15-word learning test, Stroop test, verbal fluency test, and Purdue pegboard test than healthy participants (21).

Though it is challenging to reconcile these conflicting results, the differences in the relationship between migraine and cognition could be explained by considering various factors. These include the different tests used for evaluating cognition and cognitive function, which are designed to assess different domains of understanding. Additionally, the populations from which participants are chosen in different studies, such as clinical populations or

community samples, could influence the outcome of a survey. For example, Braganza et al., in their meta-analysis, showed that migraineurs recruited from clinical settings, such as neurology clinics, tend to present with more neuropsychological deficits than those chosen from the community (14).

Furthermore, factors such as different sample sizes, ethnic populations, languages, and socioeconomic statuses of participants could contribute to these inconsistent results. It should also be noted that the adverse effects of migraine on cognition observed in our study could align with the abnormal structural changes found in previous imaging studies (6-12). Altogether, our results could support the use of cognitive function assessment tools, including the FAB, to identify probable cognitive dysfunctions in patients with migraine, particularly those with MO. These results could also be beneficial for the early identification of possible changes in these patients in the future.

The results of our study suggest that differences in sex, drinking, and smoking status have no effects on the FAB results; therefore, we did not find any relationship between these variables and cognition (Figure 2).

Regarding the relationship between years of education, age, BMI, and cognition, our study found a moderate positive correlation between years of education and a mild negative correlation between age and BMI with the FAB results, and thus cognition (Figure 1). In a similar study, Mulholland et al. demonstrated that aging could reduce gray matter density and cognition (36). Additionally, in a cross-sectional study, Mumme et al. observed that younger age and having a university education were associated with better global cognitive function (37). Furthermore, Matallana et al. investigated the relationship between cognition and education, suggesting that more years of education correlate with better performance in the MMSE results (38).

As for BMI, studies show conflicting results. For example, Lynch et al. reported that a slower rate of cognitive decline with age was observed in subjects with a BMI ≥ 27.5 kg/m² (39). However, Mwamburi and Qiu suggested that a higher BMI was associated with lower verbal IQ (40).

Another interesting result from our study was that there were no differences in the FAB results and cognition based on migraine-specific variables. In this study, differences in the frequency of migraine

headaches did not cause changes in cognition; an increase in the disease duration among migraineurs did not cause differences in the FAB results. Consistent with our findings, Rist et al. observed that after 4 - 5 years of follow-up, migraine did not cause faster cognitive decline in patients (17). However, in another study, Zhao et al. showed that increases in the duration of the disease are related to progressive brain damage in regions associated with cognition and pain processing (41).

In our study, the severity of migraine headaches did not cause more cognitive decline. Inconsistent to our findings, Kurth et al. observed that the severity of any headache could increase the volume of white matter hyperintensities (6). The history of preventive drug usage did not improve the FAB results, and therefore cognitive function. Inconsistent with our results, Borsook et al. suggested that as the insula plays a vital role in cognitive function, migraine treatments can activate and affect insular cortex function and structure (42).

5.1. Conclusions

The present study suggests that a history of migraine, especially MO, significantly reduces the FAB results, thereby indicating worse cognitive function in patients with migraine compared to healthy populations. However, these results are not observed in patients with MA, and we cannot specify the relationship between MA and cognition, nor its differences with MO. Additionally, it should be noted that the FAB results and cognition could have a moderate positive correlation with years of education and a mild negative correlation with age and BMI. Furthermore, this study found no significant differences in the FAB results and cognition based on Duration of the disease, Frequency of the disease, severity of headaches, and the history of any preventive drug use.

5.2. Limitations

The cross-sectional method used in our study could limit the precise determination of the effect migraine has on FAB results and cognition. Furthermore, the limited sample size restricts a thorough evaluation of FAB results among migraine patients and the control group; the low sample size also limits the comparison between patients with MA, patients with MO, and healthy subjects. This study was conducted in the

neurology department of Tehran Imam Khomeini Hospital clinics, which could result in socioeconomic and sampling biases. Additionally, due to financial constraints, we were unable to perform imaging evaluations of the study population.

5.3. Suggestions

Further studies are needed, as the cognitive changes in migraine patients can significantly influence their quality of life. For future research, multicenter longitudinal studies with larger patient populations could provide a more precise understanding of the cognitive effects of migraine and its subtypes. Additionally, the use of imaging modalities can help determine the specific brain regions affected by migraine and enable researchers to identify the mechanisms by which migraine impacts cognition. Furthermore, the utilization of a broader range of cognitive tests could assist researchers in evaluating the exact relationship between migraine and cognition.

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Supplementary Material

Supplementary material(s) is available [here](#) [To read supplementary materials, please refer to the journal website and open PDF/HTML].

Footnotes

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References

- Headache Classification Committee of the International Headache S. The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia*. 2013;**33**(9):629-808. [PubMed ID: 23771276]. <https://doi.org/10.1177/0333102413485658>.
- Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;**380**(9859):2163-96. [PubMed ID: 23245607]. [PubMed Central ID: PMC6350784]. [https://doi.org/10.1016/S0140-6736\(12\)61729-2](https://doi.org/10.1016/S0140-6736(12)61729-2).
- Lipton RB, Bigal ME, Diamond M, Freitag F, Reed ML, Stewart WF, et al. Migraine prevalence, disease burden, and the need for preventive therapy. *Neurology*. 2007;**68**(5):343-9. [PubMed ID: 17261680]. <https://doi.org/10.1212/01.wnl.0000252808.97649.21>.
- Stewart WF, Lipton RB, Liberman J. Variation in migraine prevalence by race. *Neurology*. 1996;**47**(1):52-9. [PubMed ID: 8710124]. <https://doi.org/10.1212/wnl.47.1.52>.
- Raval AD, Shah A. National Trends in Direct Health Care Expenditures Among US Adults With Migraine: 2004 to 2013. *J Pain*. 2017;**18**(1):96-107. [PubMed ID: 27789258]. <https://doi.org/10.1016/j.jpain.2016.10.005>.
- Kurth T, Mohamed S, Maillard P, Zhu YC, Chabriet H, Mazoyer B, et al. Headache, migraine, and structural brain lesions and function: population based Epidemiology of Vascular Ageing-MRI study. *BMJ*. 2011;**342**:c7357. [PubMed ID: 21245119]. [PubMed Central ID: PMC3022913]. <https://doi.org/10.1136/bmj.c7357>.
- Mathur VA, Khan SA, Keaser ML, Hubbard CS, Goyal M, Seminowicz DA. Altered cognition-related brain activity and interactions with acute pain in migraine. *Neuroimage Clin*. 2015;**7**:347-58. [PubMed ID: 25610798]. [PubMed Central ID: PMC4297882]. <https://doi.org/10.1016/j.nicl.2015.01.003>.
- Schmitz N, Arkink EB, Mulder M, Rubia K, Admiraal-Behloul F, Schoonman GG, et al. Frontal lobe structure and executive function in migraine patients. *Neurosci Lett*. 2008;**440**(2):92-6. [PubMed ID: 18556120]. <https://doi.org/10.1016/j.neulet.2008.05.033>.
- Wang JJ, Chen X, Sah SK, Zeng C, Li YM, Li N, et al. Amplitude of low-frequency fluctuation (ALFF) and fractional ALFF in migraine patients: a resting-state functional MRI study. *Clin Radiol*. 2016;**71**(6):558-64. [PubMed ID: 27055741]. <https://doi.org/10.1016/j.crad.2016.03.004>.
- Chen C, Yan M, Yu Y, Ke J, Xu C, Guo X, et al. Alterations in Regional Homogeneity Assessed by fMRI in Patients with Migraine Without Aura. *J Med Syst*. 2019;**43**(9):298. [PubMed ID: 31352647]. <https://doi.org/10.1007/s10916-019-1425-z>.
- Rocca MA, Ceccarelli A, Falini A, Colombo B, Tortorella P, Bernasconi L, et al. Brain gray matter changes in migraine patients with T2-visible lesions: a 3-T MRI study. *Stroke*. 2006;**37**(7):1765-70. [PubMed ID: 16728687]. <https://doi.org/10.1161/01.STR.0000226589.00599.4d>.
- Granziera C, DaSilva AF, Snyder J, Tuch DS, Hadjikhani N. Anatomical alterations of the visual motion processing network in migraine with and without aura. *PLoS Med*. 2006;**3**(10): e402. [PubMed ID: 17048979]. [PubMed Central ID: PMC1609120]. <https://doi.org/10.1371/journal.pmed.0030402>.
- Le Pira F, Reggion E, Quattrocchi G, Sanfilippo C, Maci T, Cavallaro T, et al. Executive dysfunctions in migraine with and without aura: what is the role of white matter lesions? *Headache*. 2014;**54**(1):125-30. [PubMed ID: 23808818]. <https://doi.org/10.1111/head.12158>.
- Braganza DL, Fitzpatrick LE, Nguyen ML, Crowe SF. Interictal Cognitive Deficits in Migraine Sufferers: A Meta-Analysis. *Neuropsychol Rev*. 2022;**32**(4):736-57. [PubMed ID: 34398435]. <https://doi.org/10.1007/s11065-021-09516-1>.
- de Araujo CM, Barbosa IG, Lemos SMA, Domingues RB, Teixeira AL. Cognitive impairment in migraine: A systematic review. *Dement Neuropsychol*. 2012;**6**(2):74-9. [PubMed ID: 29213777]. [PubMed Central ID: PMC5619244]. <https://doi.org/10.1590/S1980-57642012DN06020002>.
- Pellegrino Baena C, Goulart AC, Santos IS, Suemoto CK, Lotufo PA, Bensenor IJ. Migraine and cognitive function: Baseline findings from the Brazilian Longitudinal Study of Adult Health: ELSA-Brasil. *Cephalalgia*. 2018;**38**(9):1525-34. [PubMed ID: 29058954]. <https://doi.org/10.1177/0333102417737784>.
- Rist PM, Dufouil C, Glymour MM, Tzourio C, Kurth T. Migraine and cognitive decline in the population-based EVA study. *Cephalalgia*. 2011;**31**(12):1291-300.
- Pearson AJ, Chronicle EP, Maylor EA, Bruce LA. Cognitive function is not impaired in people with a long history of migraine: a blinded study. *Cephalalgia*. 2006;**26**(1):74-80. [PubMed ID: 16396669]. <https://doi.org/10.1111/j.1468-2982.2005.01001.x>.
- Rist PM, Kurth T. Migraine and cognitive decline: a topical review. *Headache*. 2013;**53**(4):589-98. [PubMed ID: 23405909]. [PubMed Central ID: PMC3618490]. <https://doi.org/10.1111/head.12046>.
- Baschi R, Monastero R, Cosentino G, Costa V, Giglia G, Fierro B, et al. Visuospatial learning is fostered in migraine: evidence by a neuropsychological study. *Neurol Sci*. 2019;**40**(11):2343-8. [PubMed ID: 31250281]. <https://doi.org/10.1007/s10072-019-03973-6>.
- Wen K, Nguyen NT, Hofman A, Ikram MA, Franco OH. Migraine is associated with better cognition in the middle-aged and elderly: the Rotterdam Study. *Eur J Neurol*. 2016;**23**(10):1510-6. [PubMed ID: 27346448]. <https://doi.org/10.1111/ene.13066>.
- Millan MJ, Rivet JM, Gobert A. The frontal cortex as a network hub controlling mood and cognition: Probing its neurochemical substrates for improved therapy of psychiatric and neurological disorders. *J Psychopharmacol*. 2016;**30**(11):1099-128. [PubMed ID: 27756833]. <https://doi.org/10.1177/026988116672342>.
- Dubois B, Slachevsky A, Litvan I, Pillon B. The FAB: a Frontal Assessment Battery at bedside. *Neurology*. 2000;**55**(11):1621-6. [PubMed ID: 11113214]. <https://doi.org/10.1212/wnl.55.11.1621>.

24. Asaadi S, Ashrafi F, Omidbeigi M, Nasiri Z, Pakdaman H, Amini-Harandi A. Persian version of frontal assessment battery: Correlations with formal measures of executive functioning and providing normative data for Persian population. *Iran J Neurol.* 2016;**15**(1):16-22. [PubMed ID: 27141272]. [PubMed Central ID: PMC4852066].
25. Barulli MR, Fontana A, Panza F, Copetti M, Bruno S, Tursi M, et al. Frontal assessment battery for detecting executive dysfunction in amyotrophic lateral sclerosis without dementia: a retrospective observational study. *BMJ Open.* 2015;**5**(9). e007069. [PubMed ID: 26338835]. [PubMed Central ID: PMC4563243]. <https://doi.org/10.1136/bmjopen-2014-007069>.
26. Osborne RA, Sekhon R, Johnston W, Kalra S. Screening for frontal lobe and general cognitive impairment in patients with amyotrophic lateral sclerosis. *J Neurol Sci.* 2014;**336**(1-2):191-6. [PubMed ID: 24239183]. <https://doi.org/10.1016/j.jns.2013.10.038>.
27. Aiello EN, Verde F, Milone I, Giacomuzzi Grigoli E, Dubini A, Carelli L, et al. The Frontal Assessment Battery (FAB) effectively discriminates between MCI and dementia within the clinical spectrum of neurochemically confirmed Alzheimer's disease. *Front Psychol.* 2022;**13**:1054321. [PubMed ID: 36533021]. [PubMed Central ID: PMC9748699]. <https://doi.org/10.3389/fpsyg.2022.1054321>.
28. Terada T, Kubota M, Miyata J, Obi T, Takashima H, Matsudaira T, et al. Frontal neurodegeneration associated with Frontal Assessment Battery in early Alzheimer's disease. *J Neurol Sci.* 2024;**467**:123327. [PubMed ID: 39608296]. <https://doi.org/10.1016/j.jns.2024.123327>.
29. Han M, Kim DY, Leigh JH, Kim MW. Value of the Frontal Assessment Battery Tool for Assessing the Frontal Lobe Function in Stroke Patients. *Ann Rehabil Med.* 2020;**44**(4):261-72. [PubMed ID: 32721991]. [PubMed Central ID: PMC7463112]. <https://doi.org/10.5535/arm.19111>.
30. Borde P, Dutta G, Singh H, Singh D, Jagetia A, Srivastava AK, et al. An analysis of neurocognitive dysfunction in brain tumors. *Indian J Psychiatry.* 2021;**63**(4):377-82. [PubMed ID: 34456351]. [PubMed Central ID: PMC8363892]. https://doi.org/10.4103/psychiatry.IndianJPsychiatry_942_20.
31. Deodato M, Granato A, Martini M, Buoite Stella A, Galmonte A, Murena L, et al. Neurophysiological and Clinical Outcomes in Episodic Migraine Without Aura: A Cross-Sectional Study. *J Clin Neurophysiol.* 2024;**41**(4):388-95. [PubMed ID: 37934069]. <https://doi.org/10.1097/WNP.0000000000001055>.
32. Rozen TD. A history of cigarette smoking is associated with the development of cranial autonomic symptoms with migraine headaches. *Headache.* 2011;**51**(1):85-91. [PubMed ID: 20553330]. <https://doi.org/10.1111/j.1526-4610.2010.01707.x>.
33. Dekker TEG, van der Heijden HS, Schirmbeck F, van Amelsvoort T, Bartels-Velthuis AA, Simons CJP, et al. The association between smoking behaviour, social cognition and social functioning in patients with a non-affective psychotic disorder: A prospective follow-up study. *Schizophr Res Cogn.* 2021;**26**:100206. [PubMed ID: 34258239]. [PubMed Central ID: PMC8259295]. <https://doi.org/10.1016/j.scog.2021.100206>.
34. Weir CB, Jan A. *BMI Classification Percentile And Cut Off Points*. Treasure Island (FL); 2025.
35. Phan MT, Tomaszewski DM, Arbuckle C, Yang S, Jenkins B, Fortier MA, et al. Evaluating the 0-10 Point Pain Scale on Adolescent Opioid Use in US Emergency Departments. *J Clin Med.* 2021;**11**(1). [PubMed ID: 35011778]. [PubMed Central ID: PMC8745662]. <https://doi.org/10.3390/jcm11010038>.
36. Mulholland MM, Sherwood CC, Schapiro SJ, Raghanti MA, Hopkins WD. Age- and cognition-related differences in the gray matter volume of the chimpanzee brain (Pan troglodytes): A voxel-based morphometry and conjunction analysis. *Am J Primatol.* 2021;**83**(11). e23264. [PubMed ID: 33899958]. [PubMed Central ID: PMC8546025]. <https://doi.org/10.1002/ajp.23264>.
37. Mumme KD, Conlon CA, von Hurst PR, Jones B, Haskell-Ramsay CF, de Seymour JV, et al. Dietary patterns and cognitive function in older New Zealand adults: the REACH study. *Eur J Nutr.* 2022;**61**(4):1943-56. [PubMed ID: 35067756]. <https://doi.org/10.1007/s00394-021-02775-x>.
38. Matallana D, de Santacruz C, Cano C, Reyes P, Samper-Ternent R, Markides KS, et al. The relationship between education level and mini-mental state examination domains among older Mexican Americans. *J Geriatr Psychiatry Neurol.* 2011;**24**(1):9-18. [PubMed ID: 20538969]. [PubMed Central ID: PMC3040264]. <https://doi.org/10.1177/0891988710373597>.
39. Lynch DH, Howard AG, Tien HC, Du S, Zhang B, Wang H, et al. Association Between Weight Status and Rate of Cognitive Decline: China Health and Nutrition Survey 1997-2018. *J Gerontol A Biol Sci Med Sci.* 2023;**78**(6):958-65. [PubMed ID: 36754372]. [PubMed Central ID: PMC10235196]. <https://doi.org/10.1093/gerona/glad051>.
40. Mwamburi M, Qiu WQ. Different associations of premorbid intelligence vs. current cognition with BMI, insulin and diabetes in the homebound elderly. *Integr Mol Med.* 2016;**3**(3):547-52. [PubMed ID: 27642517]. [PubMed Central ID: PMC5026314]. <https://doi.org/10.15761/IMM.1000202>.
41. Zhao L, Liu J, Dong X, Peng Y, Yuan K, Wu F, et al. Alterations in regional homogeneity assessed by fMRI in patients with migraine without aura stratified by disease duration. *J Headache Pain.* 2013;**14**(1):85. [PubMed ID: 24134520]. [PubMed Central ID: PMC3853130]. <https://doi.org/10.1186/1129-2377-14-85>.
42. Borsook D, Veggeberg R, Erpelding N, Borra R, Linnman C, Burstein R, et al. The Insula: A "Hub of Activity" in Migraine. *Neuroscientist.* 2016;**22**(6):632-52. [PubMed ID: 26290446]. [PubMed Central ID: PMC5723020]. <https://doi.org/10.1177/1073858415601369>.