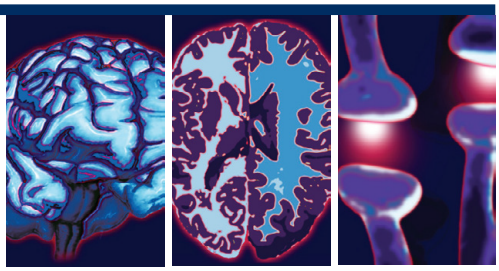
Case Report



Migraine, Major Depression and Personality Disorders: Could Obsessive-Compulsive Personality Disorder Mediate the Relationship between Migraine and Depression

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ABSTRACT

Background: Migraine is one of the most common neurological disorders. Major depression is three times more common in migraine patients than in the general population, especially among those with aura. Other personality disorders, such as obsessive-compulsive personality disorder (OCPD) and borderline personality disorder (BPD), are also suggested to be prevalent in patients with migraine. This study aims to investigate personality disorders in migraine patients and their relationship with depression.

Methods: The study included 83 patients with migraine and 63 participants without migraine, any other type of headache syndrome or neurological disorders in a control group. Demographic and clinical variables were recorded. Neurological and psychiatric examinations were conducted using the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) Structured Clinical Interview for Axis II Disorders Form, and the MIDAS (The Migraine Disability Assessment Test) score was applied.

Results: Duration of major depression was significantly longer in migraine patients than healthy controls ($p<0.001$). Major depression was more frequent in patients with migraine aura ($p<0.05$).When migraine patients with and without major depression were compared, the MIDAS score was significantly higher in patients with major depression ($p<0.05$). BPD was neither associated with the presence/absence of migraine nor the pain and attack characteristics. Family history of migraine, OCPD and histrionic and narcissistic PD were at a significantly higher frequency in patients with migraine and major depression comorbidity.

Conclusion: It seems reasonable to assume that migraine, major depression and personality disorders (most importantly OCPD) are in a close relationship, with the possibility that OCPD is a mediator between the two conditions.

Keywords: Migraine, Major depression, Personality disorders, Obsessive-compulsive personality disorder

Introduction

Migraine, a syndromic cause of debilitating headache, is one of the most common neurological disorders with a 1-year prevalence between 6–14.3% [1]. Migraine headaches are

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affected by biological, social, psychological, environmental, and family-related factors, similar to many other chronic pain disorders [2,3]. The frequency and severity of migraine has been associated with various psychiatric disorders [4], including major depression –often referred to as the migraine-major depression comorbidity. This relationship was investigated by Breslau et al. who reported that the presence of one condition could increase the likelihood of the other.

Major depression is three times more common in migraine patients than in the general population and is particularly frequent in migraine with aura than without aura. While severe headache poses a risk for major depression, there is little evidence to suggest that major depression increases migraine-related pain severity [5,6].

Many studies investigate the relationship between personality and migraine, but most of these studies have studied the relationship with personality traits rather than personality disorders [7-11]. Wolf *et al.* were the first to reveal common personality traits in migraine and had concluded that individuals with migraine expressed perfectionist, strict, orderly, ambitious, and competitive characteristics [12]. These first steps were supported by findings showing a higher frequency of personality disorders in migraine patients [13,14]. The prevalence of personality disorders in chronic headache patients was reported to be 26%, while this figure increased to 32.8% and 81% in patients with migraine and chronic migraine, respectively [13-15]. However, current evidence is conflicting with regard to the distribution and/or frequency of personality disorders in patients with migraine. Although some studies have focused on borderline personality disorder (BPD), others have put forth avoidant (AVPD) and obsessive-compulsive personality disorder (OCPD) as the prominent disorders accompanying migraine [14-15]. Despite these conflicting findings, the latest literature shows that personality disorders negatively affect the course and treatment of migraine and cause excessive drug use; indicating that the relationships are yet to bead equately explained [16].

This study aims to investigate personality disorders in migraine patients and their relationship with depression.

Materials and Methods

■ Study group

The study included 83 patients with migraine. As a control group, we enrolled 63 participants without migraine, any other type of headache syndrome or neurological disorders. Patients were eligible if they were aged between 18-70 years. Patients with tension-type headaches, epilepsy, delirium, headaches due to excessive drug use and dementia were excluded from the study. Patients were taken consecutively and neurological examinations were performed. Migraine was diagnosed by a Neurology specialist (A.Ş), according to the International Classification of Headache Disorders (ICHD-III).

■ Data collection

Psychiatric examinations of the subjects (referred to the psychiatry clinic after completion of neurological examinations) was conducted using the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) Structured Clinical Interview for Axis I Disorders Form [17,18]. Those with a psychotic disorder and physical and mental retardation that would prevent interviewing were not included in the study. Voluntarily signed, informed consent forms that had been approved by the Ethics Committee were obtained from all participants (2019/88). Demographic and clinical variables were recorded by a standardized form.

The Migraine Disability Assessment Test (MIDAS) was used to assess the degree of disability caused by migraine. A reliability and validity study of the Turkish version of the MIDAS performed by Ertaş *et al.* [19] has shown that the test was indeed reliable and valid in its Turkish form.

A Structured Clinical Interview according to DSM-IV (SCID-II) with the widely used SCID for Axis II (SCID-II) was applied. The SCID-II assessment tool consists of 113 questions and was developed for the evaluation of personality disorders [20] ;paranoid personality disorder, schizoid personality disorder, schizotypal personality disorder, antisocial personality disorder, borderline personality disorder (BPD), histrionic personality disorder, narcissistic personality disorder ,avoidant personality disorder ,dependent personality disorder and obsessive-compulsive personality disorder (OCPD). It was translated into Turkish by Sorias *et al.* [21], and the reliability/

validity study was undertaken by Coşkunol *et al.* [22]. In the face-to-face interview process, the questions are scored as absent (1), sub-threshold (2) and threshold (3). The test-retest value ofthe test was found to be k=0.68, and the interviewee's reliability value was k=0.71. Each interview lasted for about an hour.

■ Statistical analysis

Data were analyzed with SPSS version 18.0 for Windows (IBM, Armonk, NY, USA). Continuous variables were compared using the student's t-test in the presence of normal distribution of data. Differences in categorical variables were assessed by $\chi 2$ tests. A binary logistic regression model was used to determine variables independently associated with lifetime major depression diagnosis. Comparisons or relationships were considered to be significant at $p<0.05$.

Results

As depicted in **Table 1**, no significant differences were found between the migraine patients (n=83) and controls (n=62) in terms of gender, age, education and marital status. Among patients who had received major depression diagnosis, the duration of depression was 6.21 ± 4.22 months in the migraine group, while this value was significantly lower among controls (2.58 ± 2.02 years) (p=0.007). The frequency of lifetime diagnosis of depression (p=0.009) and various personality disorders, including avoidant PD, OCPD, histrionic PD, narcissistic PD and borderline personality disorder (BPD), were significantly higher in the migraine group compared to controls.

When migraine patients with and without major depression (n=33 and n=50, respectively) were compared, age of migraine onset (22.9 ± 6.2 versus 22.4 ± 6.9 years), duration of headache (27.6 ± 20.3 versus 33 ± 25.9 minutes), the number of attacks within the last 3 months (10.8 ± 10 versus 8.9 ± 6.5) and severity of headache (7.7 ± 0.9 versus 7.5 ± 0.9) were found to be similar (p >0.05).However, MIDAS score was significantly higher in patients with comorbidity (15.85 ± 8.96) compared to migraine patients without major depression (11.48 ± 7.55) (p=0.004). Additionally, all personality disorders except for schizotypal PD and antisocial PD,

Table 1: Comparison of demographic characteristics and psychiatric assessments between controls and patients with migraine.

	Migraine group (n=83)	Control group (n=62)	p-value
Age, years	40.35 ± 10.76	40.39 ± 10.98	0.98*
Duration of education, years	11.24 ± 4.34	9.76 ± 5.63	0.07*
Gender Female Male	 64 (77.1%) 19 (22.9%)	 55 (88.7% 7 (11.3%)	0.07
Marital status Married Single/Divorced/Widow	 54 (65.1%) 29 (34.9%)	 51 (82.3%) 11 (17.7%)	0.07
Family history of migraine	49 (59%)	8 (12.9%)	<0.001
Major depression	33 (39.8%)	12 (19.4%)	0.009
Avoidant PD	8 (9.6%)	1 (1.6%)	0.04
Dependent PD	6 (7.2%)	1 (1.6%)	0.11
Obsessive-compulsive PD	26 (31.3%)	2 (3.2%)	<0.001
Paranoid PD	7 (8.4%)	3 (4.8%)	0.39
Schizotypal PD	6 (7.2%)	1 (1.6%)	0.11
Schizoid PD	3 (3.6%)	0 (0%)	0.13
Histrionic PD	16 (19.3%)	2 (3.2%)	0.004
Narcissistic PD	10 (12%)	0 (3.2%)	0.005
Borderline PD	22 (26.5%)	2 (3.2%)	<0.001
Antisocial PD	2 (2.4%)	1 (1.6%)	0.73
A Cluster PD	12 (14.5%)	4 (6.5%)	0.12
B Cluster PD	25 (30.1%)	5 (8.1%)	0.001
C Cluster PD	28 (33.7%)	3 (4.8%)	<0.001
Any PD	31 (37.3%)	7 (11.3%)	<0.001

PD, personality disorder.
*Mann Whitney *U* test. All remaining comparisons performed via $\chi 2$ tests.
Bold font used to emphasize statistically significant p-values (<0.05).

Table 2: Patients with comorbid migraine and major depression compared to subjects with either migraine or major depression.

	Comorbid Migraine + MD (n=33)	Migraine without MD (n=50)	Controls with MD (n=12)	Comorbid vs. Migraine only p-value	Comorbid vs. MD only p-value
Age	42.45 ± 9.79	38.96 ± 11.24	43.83 ± 14.22	0.45*	0.38
Duration of education	10.48 ± 4.36	11.74 ± 4.29	7.83 ± 5.58	0.10*	0.91
Gender Female Male	 23 (69.7%) 10 (30.3%)	 41 (82%) 9 (18%)	 10 (83.3%) 2 (16.7%)	0.19	0.36
Marital status Married Single/Divorced/Widow	 23 (69.7%) 10 (30.3%)	 31 (62%) 19 (38%)	 7 (58.3%) 5 (41.7%)	0.47	0.47
Family history of migraine	16 (48.5%)	33 (66%)	0 (0%)	0.11	0.003
Aura	28 (84.8%)	10 (20%)	–	<0.001	N/A
Avoidant PD	7 (21.2%)	1 (2%)	1 (8.3%)	0.004	0.23
Dependent PD	6 (18.2%)	0 (0%)	0 (0%)	0.002	0.11
Obsessive-compulsive PD	24 (72.7%)	2 (4%)	2 (16.7%)	<0.001	<0.001
Paranoid PD	7 (21.2%)	0 (0%)	2 (16.7%)	0.001	0.73
Schizotypal PD	4 (12.1%)	2 (4%)	0 (0%)	0.16	0.11
Schizoid PD	3 (9.1%)	0 (0%)	0 (0%)	0.03	0.28
Histrionic PD	14 (42.4%)	2 (4%)	1 (8.3%)	<0.001	0.01
Narcissistic PD	10 (30.3%)	0 (0%)	0 (0%)	<0.001	0.09
Borderline PD	21 (63.6%)	1 (2%)	2 (16.7%)	<0.001	0.24
Antisocial PD	2 (6.1%)	0 (0%)	0 (0%)	0.07	0.22
A Cluster PD	10 (30.3%)	2 (4%)	2 (16.7%)	0.001	0.10
B Cluster PD	23 (69.7%)	2 (4%)	2 (16.7%)	<0.001	0.02
C Cluster PD	26 (78.8%)	2 (4%)	3 (25%)	<0.001	0.005
Any PD	30 (90.9%)	1 (2%)	5 (41.7%)	<0.001	<0.001

MD, major depression; PD, personality disorder; N/A, not applicable.
*Mann Whitney *U* test. All remaining comparisons performed via $\chi 2$ tests.
Bold font used to emphasize statistically significant p-values (<0.05).

were significantly more frequent in patients with comorbidity compared to migraine patients without major depression ($p<0.05$). The frequency of having a family history of migraine was also higher among migraine patients with major depression ($p<0.001$) (**Table 2**). The presence of Aura was significantly more common in comorbid disease compared to migraine only ($p<0.001$). There were no differences between subjects with and without aura in terms of pain severity (2.68 ± 1.06, 2.36 ±1.00) number of attacks (7.63 ± 0.91; 7.53 ± 0.991), MIDAS score(14.66 ± 9.19, 12 ± 7.48) and duration of depression (5.69 ± 5.92; 8 ± 4.84) ($p>0.05$).

The comparison of patients with comorbidity (n=33) and healthy subjects with major depression (n=12) showed that these groups were similar in terms of PD types, except for the OCPD ($p<0.001$) and histrionic PD ($p=0.010$); however, the presence of any type of PD was significantly higher among patients with comorbidity ($p <0.001$) (**Table 2**).

Logistic regression was performed to identify parameters that could be used for the prediction of lifetime major depression diagnosis in patients with migraine (backward conditional method). Results revealed that the age, MIDAS score and any of personality disorder were the parameters independently associated with lifetime depression (95% CI: 0.001, 0.012, p=0.031;95% CI:-0.012, 0.001, p=0.075;95% CI:-0.229, -0.008, p=0.036;95% CI:0.014,0.346, p=0.034).

Discussion

The comorbidity of migraine and major depression ranges from 8.6 to 47.9%. These results may depend on the method of research, the region or country in which the studies were performed, as well as the characteristics of the health institution (public, private, cost of treatment etc.). Our findings showed that 39.8% of migraine patients had been diagnosed with major depression throughout their lives. Considering the results of prior research, it appears that there is a two-way relationship between major depression and migraine –each being a risk factor for the other. Although other severe headaches pose a risk for major depression, there is no evidence yet that major depression is a

risk factor for these headaches. It has been shown that major depression comorbidity increases the frequency of migraine pain and further decreases life quality. Although our results demonstrated that pain frequency, severity and duration were similar in migraine patients with and without major depression; those with comorbidity had higher MIDAS scores than those with only migraine.

Similar to the literature, our results showed a higher frequency for major depression in patients with aura than in those without aura [5]. There was no difference between migraine patients with aura and those without aura in terms of other migraine characteristics, MIDAS scores and depression.

Personality disorders have been associated with medical disorders, as well as mental disorders. There is an abundance of evidence demonstrating that personality disorders are associated with cardiovascular diseases, chronic pain obesity, and HIV infection. BPD has taken a prominent role in many studies which have shown that BPD is associated with more frequent pain, migraine-related disability, medication overuse headache (MOH), hospital admission, depression, and treatment mismatch in patients with migraine. In our study, BPD was not associated with the severity of pain, duration of pain, and the number of attacks in migraine patients. However, in a study conducted the number of monthly episodes, MIDAS scores, and MOH were found to be higher in patients with BPD. BPD was the second most common personality disorder among patients with migraine in our study, similar to studies which did not find BPD as the prominent PD in migraine.

In the present study, OCPD was seen in 31.3% of migraine patients, and in 80.6% of migraine patients with any personality disorder. Similarly, OCPD was the most common personality disorder accompanying migraine in studies by Kayhan et al. (50.5%) and Yang et al. (23.0%) [14,15]. These results are consistent with the definition of a perfectionist, orderly, prescriptive and rigid migraine patient [14].

These results, despite tempting one to conclude a direct relationship between PDs and migraine, it is well-established that major depression and PD comorbidities are rather frequent, with studies identifying PD presence in 12% to 95% of patients with major depression. Therefore, it is critical to remember that the relationships suggested between migraine and various types of PD in this study may be similar to (or even caused by) the aforementioned associations between major depression and PD. For instance, the lifetime incidence of major depression in those with BPD has been reported to be 83%. Keeping this in mind, we found that patients with comorbidity of migraine and major depression had an increased likelihood of having a number of different PD types, including avoidant, dependent, OC, paranoid, schizoid, histrionic, narcissistic and borderline PDs. Our literature review did not reveal any studies investigating the relationship between PDs and major depression in patients with migraine. In order to be able to differentiate the effect of depression on the presence/absence of PDs in migraine, we performed comparisons between comorbid patients and healthy subjects with major depression. Notwithstanding the limited number of patients in the latter group, OCPD, histrionic PD and overall PD (any type) were significantly more common among patients with comorbidity; whereas there was no difference for BPD (and other types). These results suggest a relationship between migraine and OCPD, regardless of depression status.

Logistic regression with the inclusion of parameters that demonstrated a p-value lower than (or equal to) 0.1 in the comparison of migraine patients with and without major depression revealed OCPD as the only parameter that was independently associated with the likelihood of major depression in patients with migraine.

When the last two points (the OCPD–migraine and OCPD–major depression relationships) are taken together, it appears that the relationship between migraine and major depression may be mediated by the presence/absence of OCPD. However, since this is –to our knowledge– the first study on this topic, these results should be approached with caution and physicians must consider the limitations of the study when planning future investigations on this matter.

There are a number of important limitations in this study. Firstly, the number of individuals included, especially with regard to the controls with major depression group, was limited and all subjects were enrolled from a single center. In relation to this, major depression diagnoses were obtained by verbal declaration from patients and clinical characterization of

individuals were not obtained from their medical histories. Secondly, the use and application of MIDAS can be subjective and results could be affected by numerous short-term and long-term characteristics. Although all assessments were performed by a single analyst, there may have been variations from patient to patient. It is also apparent that the difference between the migraine and control group in terms of duration of major depression may have caused significant bias, and could have hampered the comparisons between the comorbidity group and controls with major depression. Lastly, suicidal ideation and/or attempts were not assessed. Such ideation are known to be exceptionally high in patients with chronic migraine, major depression and some personality disorders (including BPD). Therefore, the presence/absence of suicidal ideation may have significantly altered results.

Conclusion

All things considered, it seems reasonable to assume that migraine, major depression and personality disorders, most importantly OCPD, are in a close comorbidity-based relationship. Whether OCPD is a mediator in this relationship must be assessed in future studies that account for medical history, depression duration/severity, other comorbidities and also other factors responsible for PDs. Clinicians' awareness of these comorbidities may lessen further morbidity. Further studies may be conducted to determine the effects of affective disorders and personality on migraine and related factors, which may increase the understanding of the background of patients and could reveal new approaches to the management of patients with migraine.

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