ÖZGÜN ARAŞTIRMA ORIGINAL RESEARCH

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COMORBID PSYCHIATRIC DISORDERS IN SOME COMMON NEUROLOGICAL DISEASES

YAYGIN BAZI NÖROLOJİK HASTALIKLARDA KOMORBİD PSİKİYATRİK BOZUKLUKLAR

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Öz

Amaç
Bu çalışma, yaygın nörolojik hastalıklara eşlik eden psikiyatrik hastalıkları belirlemek amacıyla yapılmıştır.

Gereç ve Yöntem
Çalışma retrospektif bir çalışmadır. 26.12.2016 - 26.12.2017 tarihleri arasında psikiyatri polikliniğinde ayaktan tedavi gören nörolojik hastalık tanısı olan 1125 hastanın dosyaları incelendi.

Bulgular
Psikiyatri polikliniğinde ayaktan tedavi gören nöroloji hastalarında en sık depresyon (%59.9) ve anksiyete bozukluğu (%42.5) saptandı. Anksiyete bozukluğu (%63.3) migrende daha yaygındı ve depresyon en sık multiple sklerozda (%67.2) görüldü. Parkinson hastalığında kognitif bozukluk (%11,9), uyku bozuklukları (%10), Alzheimer hastalığı (%21,1) ve demans (%12,6) daha sıktı.

Sonuç
Bu çalışma, psikiyatrik bozuklukların nörolojik hastalıklara sık eşlik ettiğini desteklemektedir. Bu nedenle nörolojik hastalıklarda yaşam kalitesini artırmak için psikiyatrik değerlendirilmede gerekmektedir.

Anahtar Kelimeler: Komorbid, Psikiyatrik bozukluklar, Nörolojik hastalıklar, Yaygınlık

Abstract

Objective
This study was conducted to determine psychiatric diseases accompanying common neurological diseases.

Material and Methods
The study is a retrospective study. The files of 1125 patients diagnosed with neurologic disease who were treated as an outpatient in the psychiatry outpatient clinic between 26.12.2016 - 26.12.2017 were examined.

Results
The most commonly depression 59.9% and anxiety disorder 42.5% were diagnosed in neurology patients

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receiving outpatient treatment in the psychiatry outpatient clinic. This anxiety was more common in migraine (63.3 %) and depression was most commonly seen in multiple sclerosis (67.2%). The cognitive impairment (11.9%), sleep disorders (10%), Alzheimer's disease (21.1%) and dementia (12.6%) were more common in Parkinson disease.

Conclusion

This study supports that psychiatric disorders frequently accompany neurological diseases. Therefore, psychiatric evaluation is required in order to increase the quality of life in neurological diseases.

Keywords: Comorbidity, Psychiatric disorders, Neurological diseases, Prevalence

Introduction

Today, neurologists and psychiatrists frequently encounter comorbid psychiatric disorders in neurological diseases. The neurological diseases influence both body and mind functions, negatively affecting both the individual and his/her family, and increasing associated psychiatric disorders (1).

Studies in the literature have stated that psychiatric symptoms are often seen in almost all neurological diseases involving the central nervous system (2). According to previous studies, more than 50% of neurological patients have a mental illness that satisfies the criteria in Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV), with the most common symptoms being mood disorders, followed by cognitive and anxiety disorders (3). Studies conducted on the patients presenting to the neurology departments have shown that many neurological diseases such as stroke, seizures, Parkinson's disease and multiple sclerosis (MS) are accompanied by psychiatric disorders (4,5). The prevalence of psychiatric comorbidities was lowest in patients with cerebrovascular disease (CVD) and highest among patients with cognitive decline and epilepsy (6).

The reasons for accompanying psychiatric diseases with neurological diseases are not fully known yet. Psychopathological manifestations during can be explained by alterations in specific brain networks. Indeed, structural and functional abnormalities involving brain regions and networks entangled in the emotional-affective regulation, i.e., frontal lobes, basal ganglia, and limbic system structures, have been associated with psychiatric manifestations in neurological diseases. (7).

Psychiatric disorders that are seen frequently with neurological diseases can be treated with appropriate pharmacologic treatment or counseling. However, some studies have demonstrated that neurologists may overlook / neglect psychiatric comorbidity. İn a study conducted by the neurology department of a large hospital, 72% of psychiatric morbidity was neglected by neurologists (8). This leads to a poor quality of life in patients with neurological disease accompanied by psychiatric disorders and increased socio-economic burden (9, 10).

Studies in the literature including those from our country on this issue are limited. The objective of this study was to determine psychiatric diseases accompanying common neurological diseases and raise awareness of this problem among neurologists and psychiatrists and to reveal that neurological and accompanying psychiatric symptoms should be addressed together in treatment plans.

Material And Methods

Study design and sample

This is a retrospective descriptive study, which population comprised the files of all the patients who were treated by the psychiatry clinic on an outpatient basis between 26.12.2016 and 26.12.2017. The files of all patients were evaluated in terms of diagnosis of neurological disease (MS, epilepsy, migraine and Parkinson's disease). 1125 patients who met the inclusion criteria were included in the study. The necessary written permissions were received from the institution where the study was conducted and from the local ethics committee. All psychiatric diagnoses was made a psychiatrist in the clinic, by interviewing the patient and using Structured Clinical Interview for DSM-IV Axis I (SCID) and DSM-III-R Axis II Disorders (SCID-II).

Structured Psychiatric Interview for DSM-IV Axis I Disorders I (SCID)

It is a semi-structured clinical interview scale developed for the diagnosis of DSM-IV axis-I including clinical psychopathological conditions. This form was developed by First et al (11). Turkish validity and

reliability studies were conducted by Özkürkçügil et al (12).

Structured Psychiatric Interview for DSM-III-R Axis II Disorders (SCID-II)

It is a semi-structured clinical interview scale developed for the diagnosis of DSM-III-R Axis II Disorders including personality disorders. This form was applied for the diagnosis of personality disorders in the second axis First et al. (1995) (13). Turkish validity and reliability studies was conducted by Coskunol et al (14).

Statistical Analysis

Data were assessed using SPSS (Statistical Package for Social Science) version 15.0 statistical software. Data were analyzed using the percentage, mean and Chi-square test. The level of statistical importance in our study has been taken as $p< 0.05$.

Ethical Approval

In order to collect data, necessary approval was obtained from the Gazi University Ethics Committee (date: 26/06/2019 and number: 91610558-604.01.02) a written permission was received from and from the institution where the study was conducted, respectively.

Results

A total of 1125 patients, including epilepsy n: 428, MS n: 278, migraine 177, Parkinson's disease n: 270, were included in the study. The mean age of the patients was 48.41 ±17.77 years. The mean age was found as 42.54 ±18.71 years in epilepsy patients, 41.51±11.44 years in MS patients, 42.41±13.54 years in migraine patients and 68.04±12.90 years in Parkinson patients. There was a statistically significant difference between the disease groups in terms of age ($p<0.001$). Whereas 74.9% of all patients were female, this rate was 58.6% in epilepsy patients, 76.0% in MS patients, 85.3% in migraine patients and 51.1% in Parkinson patients.

Depression accompanied 59.9% and anxiety disorder 42.4% of the neurology patients. When the patients were evaluated in terms of the psychiatric diagnosis; it was found that anxiety disorder was most common in patients diagnosed with migraine (63.3%), followed by MS patients (54.8%), epilepsy patients (35.4%) and Parkinson patients (28.5%); respectively (Table 1, Figure1). Whereas, depression was most common in MS patients (67.2%) followed by the patients diagnosed with Parkinson (62.2%), epilepsy (56.3%) and migraine (54.8%); respectively (Table 1, Figure 2).

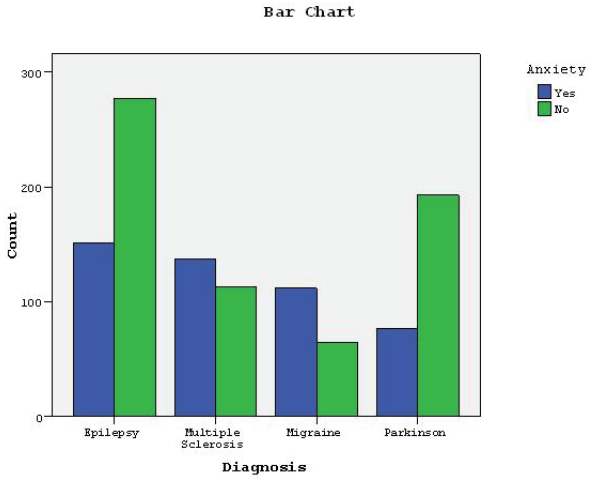

Figure 1:
Frequency of anxiety disorder in patients with neurological disorders

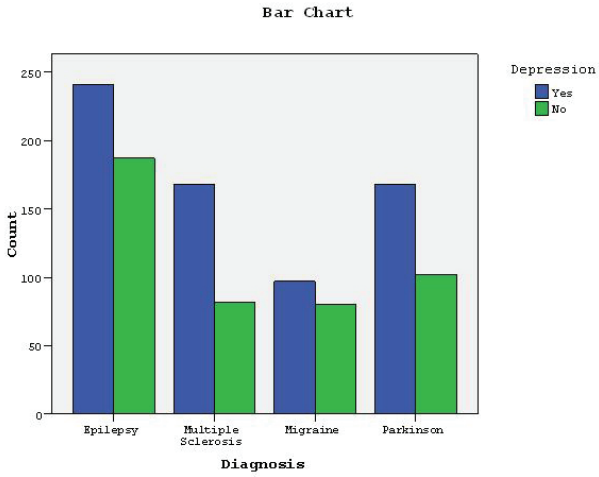

Figure 2:
Frequency of depression in patients with neurological disorders

Acute and transient psychotic disorder (ATPD) was not common in patients with neurological diseases. ATPD in this study was found in epilepsy (8.2%) and Parkinson (7.8%) patients. The most common diagnoses of mental retardation and hyperkinetic disorder were found in epilepsy patients (9.1%, 10.5%; respectively). Enuresis and activated attention disorder were seen in patients with epilepsy and MS, but not in patients with migraine and Parkinson's disease.

Cognitive impairment and sleep disturbance were statistically most common in Parkinson patients. Schizophrenia was most commonly observed in epilepsy patients followed by Parkinson, MS and

Table 1 The Descriptive Features of Neurology Patients According to the Diagnosis of Psychiatric Disorders

	Epilepsy (n=428)	MS (n=250)	Migraine (n=177)	Parkinson (n=270)
	n (%)	n (%)	n (%)	n (%)
Age	42,54 ±18,71	41,51±11,44	42,41±13,54	68,04±12,90
Female	251(58,6)	190 (76)	151(85,3)	138 (51,1)
Psychiatric Disorders				
Anxiety Disorder	151(35,4)	137 (54,8)	112 (63,3)	77 (28,5)
Depression	241(56,3)	168 (67,2)	97(54,8)	168(62,2)
Obsessive Compulsive Disorder	12(2,8)	6(2,4)	0(0)	0(0)
Bipolar Disorder	28(6,5)	10(4)	9(5,1)	25(9,3)
Acute and Transient Psychotic Disorder	35(8,2)	7(2,8)	2(1,1)	21(7,8)
Mental Retardation	39(9,1)	2(0,8)	1(0,6)	0(0)
Hyperkinetic Disorder	45(10,5)	6(2,4)	7(4)	2(0,7)
Enuresis	3(0,7)	3(1,2)	0(0)	0(0)
Cognitive Disorder	26(6,1)	4(1,6)	1(0,6)	32(11,9)
Activated Attention Disorder	3(0,7)	1(0,4)	0(0)	0(0)
Sleep Disturbance	15(3,5)	16(6,4)	7(4,0)	27(10)
Schizophrenia	21(4,9)	4(1,6)	1(0,6)	5(1,9)
Persistent delusional disorder	10(2,3)	2(0,8)	0(0)	4(1,5)
Organic delusional disorder	7(1,6)	3(1,2)	0(0)	6(2,2)
Behavioral disorder	13(3,0)	2(0,8)	1(0,6)	2(0,7)
Stuttering	3(0,7)	1(0,4)	0(0)	1(0,4)
Personality disorder	21(4,9)	12(4,8)	4(2,3)	9(3,3)
Mood disorder	12(2,8)	4(1,6)	0(0)	4(1,5)
Dissociative disorder	20(4,7)	2(0,8)	4(2,3)	3(1,1)
Somatoform disorder	8(1,9)	6(2,4)	5(2,8)	3(1,1)
Alzheimer's disease	24(5,6)	6(2,4)	0(0)	57(21,1)
Delirium	4(0,9)	1(0,4)	0(0)	6(2,2)
Panic disorder	4(0,9)	0(0)	3(1,7)	2(0,7)
Adjustment disorder	16(3,7)	10(4)	10(5,6)	2(0,7)
Dementia	22(5,1)	9(3,6)	2(1,1)	34(12,6)
Psychological developmental disorder	15(3,5)	4(1,6)	0(0)	0(0)
Post traumatic stress disorder	1(0,2)	0(0)	0(0)	1(0,4)
Eating disorder	1(0,2)	0(0)	0(0)	1(0,4)
Trichotillomania	1(0,2)	0(0)	0(0)	0(0)
Pervasive developmental disorder	4(0,9)	0(0)	0(0)	0(0)
Schizoaffective disorder	1(0,2)	0(0)	0(0)	3 (1,1)
Substance abuse	1(0,2)	0(0)	0(0)	1(0,4)
Social phobia	2(0,5)	0(0)	0(0)	1(0,4)

* All psychiatric diagnoses was made a psychiatrist in the clinic, by interviewing the patient and using Structured Clinical Interview for DSM-IV Axis I (SCID) and DSM-III-R Axis II Disorders (SCID-II).

migraine patients; respectively. Persistent (2.3%) and organic delusional disorders (1.6%) were statistically significantly higher in epilepsy patients and were not found in migraine patients. Similarly, stuttering was higher in epilepsy patients (0.7%) and behavioral disorder (3.0%) and dissociative disorder (4.7%) were the most common in epilepsy patients, Personality disorder and mood disorder were most common in epilepsy patients.

Alzheimer's and dementia diseases were most common in Parkinson patients (21.1%, 12.6%; respectively) (Table 1, Figure 3 and Figure 4). The most common diagnosis of delirium was found in Parkinson patients (2.2%), while the most common diagnosis of panic disorder was observed in migraine patients (1.7%).

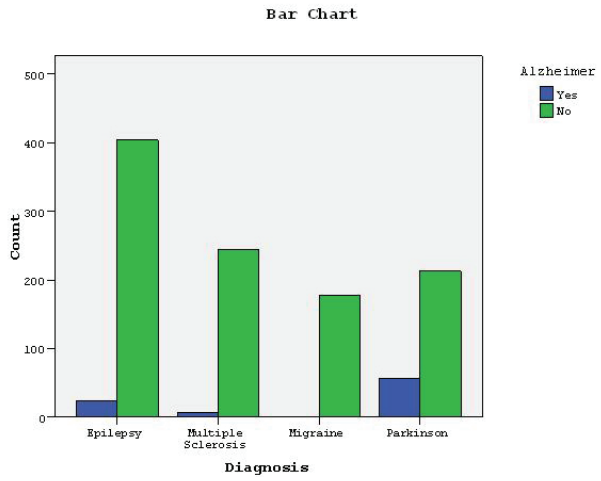

Figure 3:
Frequency of dementia in Parkinson's patients

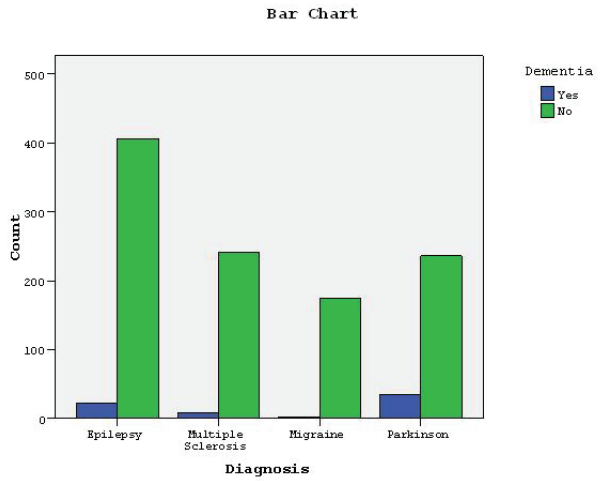

Figure 4:
Frequency of Alzheimer's disease in Parkinson's patients

Adjustment disorder was most common in migraine patients. Posttraumatic stress disorder, eating disorder, social phobia, substance abuse and schizoaffective disorder were seen only in epilepsy and Parkinson patients. Pervasive developmental disorder and trichotillomania were seen only in epilepsy patients (Table 1).

Discussion

In most neurological diseases, neurologically motor and sensory effects and psychologically cognitive, affective and behavioral effects may be seen together (6). Association of psychiatric, cognitive symptoms and neurologic signs of the underlying disease may lead to difficulty especially in the establishment of a diagnosis by neurologists or psychiatrists. In neurological diseases, psychiatric comorbidity negatively affects quality of life and physical functioning of the patient, and adaptation to the disease (15). Some psychiatric disorders (stress, depression and anxiety) are more common in some neurological diseases (16, 17). Knowing this by healthcare professionals may be helpful in the differential diagnosis attempts and, planning care and treatment in patients with neurological disease or psychiatric disease. In the present retrospective study, psychiatric comorbidities developed in patients with neurological disease were addressed.

Psychiatric disorders such as anxiety and depression are frequently seen in many neurological diseases due to the negative effects brought by the disease and treatment process to the patient and family life. In our study, most commonly depression and anxiety disorder were diagnosed in neurology patients. Anxiety is one of the comorbid psychiatric disorders seen in neurological diseases. Anxiety is seen in the majority of persons with neurological disease (6). Migraine ranks first among these diseases. In the current study, anxiety comorbidity was most commonly found in migraine patients. Looking at the literature, the rate of anxiety is high in migraine patients. This was attributed to several factors such as inability to control or stop worry, difficulty in relaxing, and worry about different things (18). Anxiety is also seen in other neurological diseases such as MS, epilepsy and Parkinson's disease (19, 20). However, it is not seen as high as in migraine disease. Depression is another comorbidity observed in neurological diseases. In our study, the rate of depression was highest in MS and Parkinson's disease (over 60%), while it was over 50% in epilepsy and migraine.

It is stated that bipolar disorder, suicide attempt, anxiety, and depression are comorbid psychiatric

disorders in MS patients and its incidence is higher in these patients compared to the normal population. This higher incidence is reported to be resulted from psychosocial factors such as the progressive course of the disease and resulting in serious functional loss. In addition, as a result of the known pathophysiology of the disease, treatments administered are thought to form a basis for psychiatric disorders (21). Cerebral lesions and autoimmune factors have also been held responsible for the etiology of depression, which is among the most common symptoms in MS (21). In a study by Hanna and Strober, depression in MS patients was found to be associated with social support, substance abuse and education status (22).

High depression level in Parkinson's disease has been associated with pain, constipation and gastrointestinal disorders (23). The most commonly seen disorder in Parkinson patients is depression with an incidence of 17-50%. Whereas, anxiety disorders are seen by 40-82% in these patients. Previous studies have shown that the number of depression and anxiety cases increase as the stage and duration of the disease increase (24). Depression seen in Parkinson patients may be associated with the advanced age of the patients, a reaction to the realization of period and disease emotional losses, decreased density of neurotransmitters such as dopamine, serotonin, noradrenaline because of the striatal, mesolimbic and mesocortical involvement during the disease, and drugs used in the treatment (25).

Studies evaluating anxiety and depression disorders in migraine patients have reported that painful physical symptoms cause anxiety and depression in patients and impair quality of life (26, 27). In another study, a high rate of depression in migraine patients was associated with headache (28). It has been stated that the high rate of depression among epilepsy patients may be associated with the treatment regimen and the use of single or multiple drugs (29).

In parallel with our study, studies in the literature reported a high rate of obsessive compulsive disorder (OCD) in epilepsy patients. This was attributed to the drugs used, affected region and temporal region seizures (30). Consistently with the literature, in our study the rate of OCD was high among MS patients. The reasons for this include a high level of disability, duration of the disease, and the involvement of cranial, cerebellar, sensory and motor nerves (31). Although in the present study OCD was not found in Parkinson diseases, there are contrary studies in the literature reporting OCD in Parkinson (32). OCD seen in Parkinson patients was stated to be associated with the left side involvement or bilateral motor disorder (33). Unlike this study, it has been reported that OCD is observed also in migraine patients and this is associated with age, gender, income level, race and pain frequency (34). Cognitive disorders are commonly seen in Parkinson's disease, epilepsy, MS and other neurological diseases. However, the rate of cognitive disorder is higher in Parkinson's disease. It was stated that this is related to factors such as the observation of Parkinson's disease in older ages, the activity level in the youth, and smoking (34).

It is stated that dementia is frequently seen in Parkinson patients, and 50% of these patients develop dementia within the first 10 years after being diagnosed with Parkinson. Alzheimer's disease and Parkinson's disease are the most common two neurodegenerative diseases. Both diseases are seen over 40 years of age and especially in advanced ages, and the main cause of dementia is Alzheimer (35). In our study, most patients aged over 40 years and dementia was most commonly found in Parkinson patients.

In addition, in our study the rate of sleep disturbance was statistically significantly higher in Parkinson patients. Similarly, it has been stated that sleep disturbances are frequently seen in Parkinson patients, sleep is markedly interrupted in polysomnographic studies, sleep efficiency is decreased, and sleep disorders such as REM (Rapid-Eye-Movement) behavior disorder and periodic movement disorder in sleep are more common in Parkinson patients compared to the general population (36). Parkinson patients show worsening by the progression of sleep disturbance and it was reported that this is pathophysiologically closely related to nigrostriatal dopamine loss (37). In addition, it was stated that sleep disturbance developed in Parkinson patients caused by snoring at night, difficulty in breathing and urination (38). Several sleep disorder such as insomnia and daytime drowsiness may be seen in Parkinson patients due to both the disease itself and the drugs used (26). Studies have shown that the prevalence of sleep disturbance is between 65-95% in Parkinson's disease and this rate increases as the disease progresses (39).

In parallel with our study, it was reported in a study that mental retardation is most commonly seen in epilepsy patients and this was shown to be caused by seizures experienced (40). Psychotic disorders are also more common in epilepsy patients compared to other diseases. This was demonstrated to be caused by antiepileptic drugs used (41). Consciousness disorders seen in epilepsy patients were associated with the post-seizure damage (42).

Schizophrenia is another comorbidity seen in neurological diseases. Schizophrenia is most commonly seen in epilepsy among patients with epilepsy, MS, migraine and Parkinson's disease. Although this result varies in ratio, it is similar among the studies (43). Psychosis symptoms in epilepsy patients were associated with status epilepticus, a history of psychosis symptoms, psychiatric disorder and the use of some drugs (44). Although delusional disorders are infrequent, they are observed in neurological diseases. Although a comprehensive study could not be found on this issue, delusional disorders in epilepsy have been studied as a case report (45). Behavioral disorders are more frequently seen in epilepsy patients compared to the general population and patients with other neurological diseases. Also in our study the frequency of behavioral disorders was higher in epilepsy patients compared to the patients with MS, Parkinson's disease and migraine. Behavioral disorders in epilepsy patients were associated with the drugs used, cerebral damage, the affected area and personality traits (46). In the current study, behavioral disorder was more common in epilepsy than in the other diseases. This may be associated with the high prevalence and lack of diagnosis of depression in epilepsy patients.

Mood disorder is one of the most commonly seen psychiatric disorders in epilepsy. Among mood disorders, depression is common in epilepsy patients, although anxiety and bipolar disorder can also be observed in epilepsy patients. Mood symptoms are thought to manifest in relation with seizures in epilepsy patients. Some epileptic persons may experience a depressive mood immediately after the seizure (namely in postictal state). It was reported that in some cases, hypomania or other manic symptoms may occur just before and after seizures (47). Although dissociative disorder is not a commonly seen disorder, it can be observed in epilepsy patients. In our study, the rate of dissociative disorder was higher in epilepsy compared to the other neurological diseases. Since posttraumatic stress disorder, dissociative disorders, and psychogenic seizures are often comorbid diagnoses in patients with epilepsy. Traumatic effect and associated dissociative disorder dimension of epilepsy should be included in the psychiatric approach (48). In a study by Ahmadvand et al., the rate of epilepsy was 1% in a group in which dissociative disorder was seen by 3.4% (49).

Alzheimer's disease is among the most frequently seen disorders in neurological diseases. Parkinson and Alzheimer are the two most commonly seen neurodegenerative diseases due to the similar clinical and pathophysiological features of Parkinson's and Alzheimer's diseases (50).

Although no study could be found showing the relationship between adjustment disorder and Parkinson's disease, epilepsy, MS and migraine; it is thought that adjustment disorder seen with these diseases may be associated with anxiety and depression. Because the rates of anxiety and depression are higher in this group of patients. Dementia is more commonly seen in neurodegenerative diseases. This can explain dementia seen in epilepsy. In the present study, dementia ranked second in epilepsy patients. Looking at the literature, dementia is seen in epilepsy patients, while at the same time epilepsy is seen in dementiapatients. It is not clear which affects the other, although both diseases influence each other (51, 52).

Problems such as attention disorder and altered cognitive processes are the other conditions observed in epilepsy patients (53-55). It is stated that neuropsychiatric disorders are seen in epileptic patients due temporary or permanent problems caused by seizure activity in the structures related to mental functions, development, connections and metabolisms of these structures (56, 57). It has been shown that repetitive seizures cause mental problems through various mechanisms. This result has been confirmed by studies conducted on children diagnosed with epilepsy, reporting that learning disabilities, attention deficit hyperactivity disorder, mood disorder and anxiety were seen in some of these children (57).

Limitations

The records in the study were examined only in terms of MS, Parkinson's, epilepsy and migraine diseases. Psychiatry patients have been evaluated in terms of these four diseases, since it has been discussed more that psychiatric symptoms are common in these diseases in the literature. Stroke patients, a very common neurological disease, were not included in the study. Because psychiatric symptoms change over time after a stroke. It has also been reported that the prevalence of psychiatric comorbidities in stroke patients is low compared to other neurological diseases. It is also anticipated that it will facilitate the examination of the records. Another limitation of our study is the lack of evaluation according to age and gender distribution.

Conclusion

Many psychiatric disorders are seen with neurological diseases. This study was demonstrated that OCD, acute or transient psychotic disorder, mental retardation, hyperkinetic disorder, schizophrenia,

persistent delusional disorder, behavioral disorder, mood disorder, dissociative disorder, and psychological development disorder were more commonly seen in epilepsy patients compared to the patients with the other diseases. Whereas, cognitive impairment, sleep disorders, Alzheimer's disease and dementia were more common in Parkinson disease. Although other disorders are also seen, anxiety and adjustment disorder were more common in migraine. Depression was most commonly seen in MS. This study was showed that health professionals should not overlook comorbid diseases in the diagnosis, treatment and care of neurological patients.

This study supports the opinion that comorbid psychiatric disorders are frequently seen with neurological diseases. The results of this study indicate that neurology patients should receive more effective care and treatment, they should be assessed also from psychiatric aspects in their routine examinations to increase their quality of life and whether the underlying pathology associated with a psychiatric disorder should be investigated.

Conflict of Interest Statement
The authors have no conflicts of interest to declare.

Ethical Approval
All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with Declaration of Helsinki in 1995 (as revised in Brazil 2013) and its later amendments or comparable ethical standards. The necessary approval was received from Ethics Committee (Gazi University ethics committee, dated 26.06.2019 and numbered 91610558-604.01.02).

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Availability of Data and Materials
Data available on request from the authors

Editorial Board Membership
GK is editorial board member of the journal, but he did not take any part in the editorial processes of this article.

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