DOI: 10.5455/bcp.20120731060406

Affective Temperaments in Epilepsy

Esra Yazici[1], Ahmet Bulent Yazici[2], Nazan Aydin[3], Asuman Orhan Varoglu[4], Ismet Kirpinar[5]

ÖZET:

Epilepside affektif mizaç özellikleri

Amaç: Epilepside özellikle depresyon olmak üzere sıklıkla görülen duygudurum bozuklukları (DDB), hastalığın takip, tedavi ve seyri açısından olumsuz sonuçlara neden olabilmektedir. Duygudurum bozukluklarının etiyolojisi araştırılmaya devam edilmekte olup, risk grupları tanımlanmaya çalışılmaktadır. Affektif mizaç özellikleri günümüzde duygudurum bozukluğunun öncülleri olarak düşünülmektedir. Bu çalışmada affektif mizaç özelliklerinin epilepsili hastalarda duygudurum bozukluğunun muhtemel öngördürücüsü olup olmadığını incelemeyi amaçladık. Böylece epilepsi-duygudurum bozuklukları komorbiditesine yaklaşım icin öncül parametreleri belirlemek üzere bir adım oluşturmayı hedefledik.

Yöntem: 73 epilepsili hasta ve 79 sağlıklı kontrol bu çalışmaya dahil edilmiş daha sonra Memphis, Pisa, Paris ve San Diego Mizaç Değerlendirme Anketi'nin Türkçe formu (TEMPS-A) ve SCID-I formları kullanılarak hastalar değerlendirilmiştir.

Bulgular: Epilepsi hastaları hipertimik mizaç hariç tüm affektif mizaç özelliklerinde yüksek puanlara sahiptiler. Epilepsili hastalarda anksiyöz ve irritabl mizaç daha yüksek oranda gözlenmiştir ve anksiyöz mizaç major depresif bozukluk (MDB) ile bağlantılı bulunmuştur. Epilepsi grubunda 14 hastaya kontrol grubunda ise 6 hastaya MDB tanısı konuldu. Anksiyöz mizaç epilepsili hastalarda MDB için öngördürücü olarak tespit edildi.

Sonuç: Epilepsi hastalarında duygudurum bozukluğuna eğilim olduğu bilinmekteydi ancak bu çalışmada ilk defa epilepsi hastalarında 'affektif mizaç'a eğilim olduğu gösterilmiştir. Epilepside başta depresyon olmak üzere duygudurum bozuklukları sıklıkla komorbid olarak görülmekte olup hastalığın seyrini ve tedavisini olumsuz olarak etkileyen bir durum olarak karşımıza çıkmaktadır. Epileptik olan kişilerde duygudurum bozukluğunun öngördürücülerinin belirlenmesi riskli gruplara özel bir yaklaşımı ve prognozun daha iyi olmasını sağlayabilir.

Anahtar sözcükler: Epilepsi, affektif mizaç, depresyon, duygudurum bozuklukları

Klinik Psikofarmakoloji Bülteni 2012;22(3):254-61

ABSTRACT:

Affective temperaments in epilepsy

Objective: Mood disorders (MDs), particularly depression, are often encountered in epilepsy and may negatively affect the treatment and prognosis of the disease. Investigations into the etiology of MDs and the qualities of at-risk groups have revealed that affective temperament characteristics are antecedents of MDs. In this study, our objective was to investigate whether affective temperament characteristics were predictors of MDs in epilepsy patients. Thus, we aimed to establish a first step to determine preliminary parameters for an approach to the comorbidity of epilepsy and MDs.

Methods: In total, 73 epilepsy patients and 79 healthy controls were included in this study. The participants were evaluated using the Turkish version of the Temperament Evaluation of Memphis, Pisa, Paris, and San Diego Autoquestionnaire (TEMPS-A) and the Structured Clinical Interview of DSM Disorders (SCID-I).

Results: Epilepsy patients produced high scores in all affective temperament characteristics except hyperthymic temperament. Anxious and irritable temperaments were observed more frequently in epilepsy patients, and anxious temperament was found to be associated with major depressive disorder (MDD). Fourteen participants in the epilepsy group and 6 participants in the control group were diagnosed with MDD. Anxious temperament was determined to be a predictor of MDD.

Conclusion: Although it has been shown previously that epilepsy patients tend to suffer from MDs, for the first time, this study has demonstraed that epilepsy patients also tend to have affective temperaments. MDs, particularly depression, are frequently observed in epilepsy patients as comorbid disorders, and they have an adverse effect on epilepsy treatment and prognosis. Determining the predictors of MDs in epilepsy patients may improve the current approach toward at-risk groups and lead to better prognoses.

Key words: Epilepsy, affective temperament, depression, mood disorders

Bulletin of Clinical Psychopharmacology 2012;22(3):254-61

This study was presented as a preliminary study at EPA-2010-Munich-Germany as a proceeding.

[1]M.D., Service of Psychiatry, Derince Training and Research Hospital, Kocaeli - Turkey
[2]M.D., Department of Psychiatry, Kocaeli Seka State Hospital, Kocaeli - Turkey
[3]M.D., Department of Psychiatry, School of Medicine, Atatürk University, Erzurum - Turkey
[4]M.D., Department of Neurology, Selçuklu School of Medicine, Selçuk University, Konya - Turkey
[5]M.D., Department of Psychiatry, School of Medicine, Bezmialem University, İstanbul - Turkey

Yazışma Adresi / Address reprint requests to: Dr. Esra Yazıcı, Service of Psychiatry, Derince Training and Research Hospital, Kocaeli - Turkey

Telefon / Phone: +90-262-317-8000

Elektronik posta adresi / E-mail address: dresrayazici@yahoo.com

Gönderme tarihi / Date of submission: 1 Mayıs 2012 / May 1, 2012

Kabul tarihi / Date of acceptance: 31 Temmuz 2012 / July 31, 2012

Bağıntı beyanı:
E.Y., A.B.Y., N.A., A.O.V., I.K.: Yazarlar bu makale ile ilgili olarak herhangi bir çıkar çatışması bildirmemişlerdir.

Declaration of interest:
E.Y., A.B.Y., N.A., A.O.V., I.K. : The authors reported no conflict of interest related to this article.

INTRODUCTION

Mood disorders (MDs), particularly depression, are frequently observed in epilepsy patients (1) and have a negative effect on the treatment and prognosis of epilepsy, requiring an integrated approach (2). Identifying individuals at risk of MDs may enable an earlier and different approach to epilepsy patients with comorbid disorders. It has been shown that MDs, especially depression, are seen in epilepsy more frequently than other chronic diseases and have a negative effect on the patient's adaptation to treatment, frequency of seizures, and quality of life, and increase the risk of suicide. Furthermore, epilepsy patients often do not mention depressive symptoms, and depression can be overlooked in such patients. This indicates the necessity of a more sensitive approach to MDs in epilepsy patients (3-5).

Genetic, biological, and psychosocial approaches dfor identifying the etiology of MDs and at-risk groups exist. Akiskal claims that affective temperaments form the basis of MDs and defines five main affective temperaments (6) in a model aimed at identifying individuals at risk of MDs (7-11). It has recently been determined that depressive temperament is associated with frequent, recurrent, and severe depression that begins early; hyperthymic temperament is associated with bipolar disorder; and cyclothymic temperament is associated with early onset depression (12, 13). Genetic studies suggest that familial transmission of affective temperaments may occur (14).

This study investigated affective temperament characteristics and related factors with the intention of shedding light on the evaluation of at-risk groups and the probable common etiology for epilepsy–MD comorbidity.

MATERIALS AND METHODS

This study was carried out on outpatients diagnosed with epilepsy at the Epilepsy Clinic in the Neurology Department of a university hospital. All participants, who signed written informed consent, were chosen sequentially, and the ones meeting exclusion criteria were excluded.

The study was approved by the Ministry of Health, Erzurum Provincial Directorate of Health Ethics Committee, on April 17, 2009, and numbered 3/92. The patients were interviewed and their diagnoses were confirmed with the Structured Clinical Interview of DSM Disorders (SCID). Following this, the Turkish version of the Temperament Evaluation of Memphis, Pisa, Paris and San Diego Autoquestionnaire (TEMPS-A) and the epilepsy information form were applied.

The inclusion criteria were as follows: a diagnosis of epilepsy for at least six months, agreement to participate in the study, sufficient literacy to take the tests, and being in the age range of 16-65 years. Exclusion criteria were as follows: suffering from a cognitive disorder (e.g., mental retardation or dementia) that might affect the accuracy of test answers, suffering from an organic disorder (e.g., a tumor in the frontal lobe) that might be directly associated with epilepsy or the patient's personality, and the use of alcohol or drugs.

An information form prepared by the researchers was used to gather sociodemographic information of patients and the clinical features of epilepsy. After obtaining the consent of the participants included in the study, the epilepsy data form was completed, and the SCID-I was carried out by a psychiatrist. Following the interview, the participants were given the TEMPS-A tests, and the results were evaluated.

Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) and Structured Clinical Interview for DSM-IV Axis I Disorders, Clinical Version (SCID-CV)

The SCID-I is a partially structured diagnostic interview containing the DSM-IV diagnoses, translated to Turkish and confirmed for validity/reliability by Çorapçıoğlu et al. (1999). It starts with a sociodemographic data guide and covers seven psychiatric diagnosis groups. It is highly reliable for diagnosing serious psychiatric disorders, and it is used as a standard interview in clinical studies to confirm diagnoses (15,16).

Turkish Version of the Temperament Evaluation of Memphis, Pisa, Paris, and San Diego Autoquestionnaire (TEMPS-A)

The TEMPS-A, developed in 1997 by Akiskal et al., is used to evaluate average scores for dominant affective temperament and sub-types of affective temperament. The validity/reliability of the Turkish version of the scale, which consists of 99 items, was confirmed by Vahip et al.

It is a Likert-type self-evaluation scale and comprises five sub-dimensions assessing depressive, cyclothymic, hyperthymic, irritable, and anxious temperaments (17).

Statistical Analyses

The statistical analysis was carried out using SPSS 13.0 for Windows. A chi-square (χ^2) test was used for the comparison of the epilepsy and control groups for the evaluation of gender, profession, marital status, drug use history, psychiatric diagnosis, and affective temperament types.

In evaluating formal education, groups were established for 8 years or less, 8-15 years, and 16 years or more. To evaluate the relationship between education and affective temperament, one-way ANOVA and post-hoc Scheffe tests were applied.

A Student's t-test was used for the comparison of genders and groups for average age, disorder onset age, frequency of seizures, and the TEMPS-A point averages of the groups. Pearson correlation analysis was used to evaluate the relationship between age and TEMPS-A point averages.

A one-way ANOVA was used for the evaluation of the relationship between frequency of seizures and temperament characteristics of epilepsy patients, and a post-hoc Scheffe test was used for an advanced analysis between sub-groups. Multiple linear regression analysis was used to determine whether epilepsy and its prognosis were predictors of affective temperament characteristics according to TEMPS-A scale scores.

In preparing the regression models, variables, factors reported in the literature as influencing affective temperaments, and statistical significances obtained in previous steps were considered. Dummy variables were created for parameters such as gender, presence of epilepsy, and presence of MDD.

RESULTS

In total, 152 participants aged 16-65 years were included in the study, 73 in the epilepsy group and 79 in the control group. The average age of the epilepsy group was 25.8±9.5, and the average age of the control group was 27.7±8.2. The difference between the average ages was not significant (p=0.19). There were 36 men and 37 women in the epilepsy group and 43 men and 36 women in the control group. The chi-square test revealed no significant difference between the two groups (p=0.53). In terms of marital status, 48 participants in the epilepsy group were single and 25 were married, while in the control group, 52 were single and 27 were married. The chi-square test revealed no significant difference between the two groups (p=0.99). Regarding formal education, in the epilepsy group, the number of individuals who had received <8 years, 8-15 years, and >16 years of education were 25, 35, and 13, respectively. In the control group, these figures were 16, 36, and 27, respectively, indicating that the individuals in the epilepsy group had a lower level of education ($p<0.05$).

Evaluation of Affective Temperaments and Related Factors

While 15 depressive, 5 cyclothymic, 11 irritable, and 8 anxious temperaments were detected in the epilepsy group, only 4 depressive, 4 irritable, and 4 anxious temperaments were detected in the control group. The higher results for depressive temperament (p=0.004) and irritable temperament (p=0.034) were statistically significant. No hyperthymic temperaments were detected in either group.

An evaluation of the groups according to their average TEMPS-A point averages revealed that the depressive ($p<0.001$, t=-4.28), cyclothymic ($p<0.001$, t=-4.67), irritable ($p<0.001$, t=-5.21), and anxious temperament ($p<0.001$, t=-4.49) scores of the epilepsy group were significantly higher than those of the control group. However, there was no significant difference in hyperthymic temperament scores (p=0.72, t=0.35) (Figure 1).

In all samples, a positive correlation was found between age and depressive temperament scores (r=0.261, p=0.01). Women had higher anxious and cyclothymic temperament scores than men. The depressive temperament scores of married persons were higher than those of singles (married=8.25, single=6.63, t=-2.26, p=0.026). Furthermore, the one-way ANOVA carried out for level of education showed that those with lower levels of education had higher depressive, cyclothymic, and irritable temperament scores.

In the epilepsy group, cyclothymic temperament scores in women (p=0.027, t=2.26) and single participants

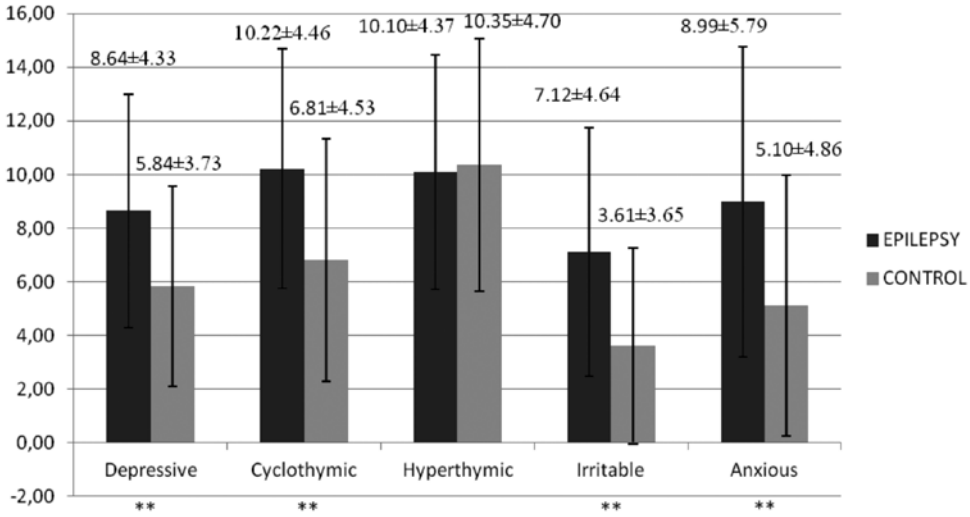

Figure 1: Comparison of the average TEMPS-A scores of the epilepsy and control groups
**: p<0.001

Table 1: Predictors obtained through multiple linear regression analysis of TEMPS-A scores

	Epilepsy	Gender	Marital Status	Education	MDD	R^2
Depressive						
beta	-0.244	-0.161	0.168	-0.164	0.262	0.255
P	**0.001**	**0.049**	**0.032**	**0.030**	**0.001**	
Cyclothymic						
beta	-0.267	-0.192	-0.066	-0.207	-0.213	0.247
P	**0.000**	**0.012**	0.378	**0.007**	**0.005**	
Hyperthymic						
beta	-0.011	-0.011	0.034	0.014	-0.215	0.045
P	0.899	0.894	0.688	0.865	**0.011**	
Irritable						
beta	-0.335	0.052	-0.018	-0.047	0.288	0.240
P	**0.000**	0.496	0.811	0.532	**0.000**	
Anxious						
beta	-0.236	-0.206	0.060	-0.159	0.380	0.333
P	**0.001**	**0.004**	0.393	**0.026**	**0.000**	

(p=0.037, t=2.12) were significantly higher (p<0.05). MDD (p=0.035, χ^2=4.455), and social phobia (p=0.002, χ^2=9.941) was significantly more frequent in epilepsy patients. Furthermore, the number of individuals with a psychiatric diagnosis was significantly higher in the epilepsy group than in the control group (epilepsy: n=27, control: n=9, p<0.001, χ^2=13.750).

In both groups, presence of MDD was evident. In all samples, depressive (p<0.001, t=-4.64), cyclothymic (p=0.001 t=-3.53), irritable (p<0.001, t=-4.53), and anxious (p<0.001, t=-6.24) temperament scores were significantly higher in the group with the MDD diagnosis.

A regression model was prepared to determine predictors of affective temperament scores in all samples. Accordingly, the multiple linear regression model (comprising independent variables such as the presence of epilepsy, gender, marital status, level of education, and the presence of MDD) was applied separately for each affective temperament score (Table 1). This model demonstrated that the presence of an epilepsy diagnosis was an independent predictor of the differences between the depressive, cyclothymic, irritable, and anxious temperament scores. Gender was a predictor of depressive, cyclothymic, and anxious temperament scores; level of

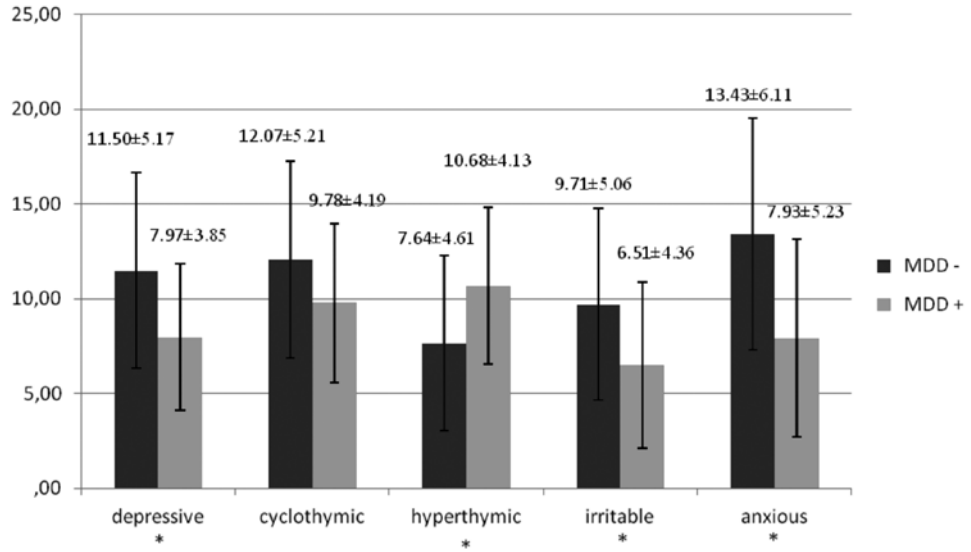

Figure 2: Comparison of the affective temperament scores of depressive and not depressive patients
*: p<0.05, MDD- : not depressive group, MDD+ : depressive group

Table 2: Clinical Findings of Epilepsy Patients

Average age of first seizure	(1- 63)	18.1 ± 10.6
Aura	Yes	n=35 47.9%
	No	n=38 52.1%
Frequency of Seizure	<15 days	n=16 21.9%
	Once a month	n=8 11%
	Once every 3 months	n=12 16.4%
	Once every 6 months	n=7 9.6%
	Once a year or less	n=28 38.2%
Average Duration Of Disease (years)	(1-32)	7.72 ± 7.82
Seizure Type	Partial seizure	n=7 9.5%
	Generalized Seizure	n=66 90.5%

education was a predictor of depressive, cyclothymic, and anxious temperament scores; and MDD was a predictor of all temperament scores.

Relation of Depression with Affective Temperaments in the Epilepsy Group

It was observed that those with MDD in the epilepsy group had higher depressive (p=0.005, t=2.87), irritable (p=0.019, t=-2.29), and anxious (p=0.001, t=-3.42) temperament scores and lower hyperthymic (p=0.018, t=2.41) temperament scores than those without (Figure 2). Similarly, patients with both epilepsy and MDD had a more frequent occurrence of depressive, cyclothymic, and anxious temperaments (p<0.05).

Clinical Findings Regarding Epilepsy

The clinical characteristics of the epilepsy patients regarding their epilepsy are given in Table 2. No significant correlation was found between age at first seizure, duration of illness, presence of auras, type of seizures, or affective temperament characteristics.

A one-way ANOVA was applied to determine the relationship between the frequency of seizures and temperamental characteristics of epilepsy patients, and a significant difference was detected in depressive temperament among the TEMPS-A parameters. An advanced analysis using the post-hoc Scheffe test showed that the groups causing the significant difference in depressive temperament were the group that had seizures

"more than once every 15 days" and the group that had seizures "less than once a year" ($p<0.05$).

A multiple linear regression model wasformed with clinical epilepsy characteristics (e.g., duration of illness, type of seizures, frequency of seizures, and gender), MDD, and marital status as independent variables. In this model, duration of illness ($\beta=0.226$, $p=0.036$, $R^2=0.304$), frequency of seizures ($\beta=0.375$, $p=0.001$), and depression ($\beta=0.226$, $p=0.043$) were predictors as independent variables. On the other hand, only the presence of MDD ($\beta=0.345$, $p=0.004$, $R^2=0.223$) was a predictor of anxious temperament.

DISCUSSION

In this study, among the affective temperaments accepted as the antecedents of MDs and important for determining at-risk groups , the presence of depressive and irritable temperaments and the depressive, cyclothymic, irritable, and anxious temperament scores in the epilepsy group were found to be significantly higher than those of the control group.

Recent studies show that affective temperament types are subsyndromal indications and antecedents of MDs (12). Irregularities in temperament are a familial genetic characteristic for a tendency to manic-depressive episodes (18). It has been stated that the probability of a dominant affective temperament in persons with a history of affective disorders in the family is two-fold (19). In a study investigating the relation between affective temperaments and MDD, it was disclosed that there was a strong correlation between cyclothymic, depressive, and anxious temperaments and inherited depression (19). Another study revealed that high depressive temperament scores were related to recurrent depressive disorder, and high hyperthymic and cyclothymic temperament scores to bipolar disorders and psychotic features that accompany bipolar disorder (20). In our literature review, no study was found on the evaluation of affective temperament in epilepsy patients. This study has shown, for the first time, that epilepsy patients not only tend to suffer from MDs, but also tend to have affective temperaments that put them at risk for MDs.

Psychiatric Diagnosis Distribution in the Epilepsy and Control Groups

The most frequently observed comorbidities in the epilepsy group were depressive disorders led by MDD and followed by anxiety disorders, which is supported by the literature (21). Social phobia, not mentioned before in the literature, was significantly more common in the epilepsy group than in the control group. The distribution of other diagnoses in the control group were in conformance with literature (22).

This study has shown that in the epilepsy group, both affective temperament diagnoses and depression were more frequent than in the control group. In epilepsy patients, especially in frontal lobe epilepsy patients, MDs are observed frequently, the most common being depression (21). Recent research has shown a decrease in the volume of the hippocampus, a part of the limbic system, in individuals suffering the depression that follows epilepsy surgery, which begs the question of whether or not there are common anatomical areas affected by both epilepsy and depression (23). Understanding the neurobiological causes underlying temperament will be a key to understanding psychological disorders. One study has shown that specific areas of the prefrontal cortex (the dorsolateral prefrontal, anterior cingulate, and orbitofrontal cortex) and the limbic system are associated with the three main dimensions of temperament, namely, negative affect, positive affect, and constraint (24). The diagnoses and scores determined for epilepsy patients in this study may be associated with the increased MD frequency in epilepsy patients, suggesting a common neuroanatomical pathology, particularly in the limbic system, besides a common genetic tendency to MDs.

Association of Depression with TEMPS-A Scores

In the epilepsy group, depressive, cyclothymic, and anxious temperament numbers and scores were higher for patients diagnosed with MDD comorbidity, and MDD was a predictor of high depressive, irritable, and anxious temperament scores, independent of epilepsy. This is in line with the study of Lazary et al., which investigated the association of affective temperaments with MD and discussed the association of anxious, depressive, and cyclothymic temperaments with high depression scores (19). Through the current study, it can be said that the findings are also valid for the epilepsy group. The study carried out by Bostanci et al., showing the clinical findings that become dissimilar when major depression accompanies

epilepsy, also supports our findings (25). However, the small number of cases in our study prevents the hypotheses from being fully proven.

Association of Clinical Findings and Personality Traits of Epilepsy Patients

In this study, the depressive temperament scores of those having frequent seizures were higher than those who had seizures once a year or less. Long illness duration and frequent seizures in epilepsy are associated with higher degrees of atrophy in white and gray matter (25).

It could be reasoned that individuals who have frequent seizures have a harder time adapting to and participating in social groups and feel rejected (26), which may lead to higher depression scores. Moreover, more frequent seizures may have caused a higher degree of organic damage and a tendency to depressive temperament due to social interaction in our participants. As mentioned, depressive temperament may be a predictor of depression.

In this study, the association of MD, epilepsy, psychiatric comorbidity, and affective temperament in epilepsy patients was investigated, and epilepsy patients were found to have higher depressive, cyclothymic, irritable, and anxious temperament scores. Furthermore, anxious temperament in epilepsy patients was found to be a predictor of MDD.

This study has formed a basis for the understanding of affective temperament and associated factors in epilepsy. Affective temperaments have increasing value in identifying groups at risk for MDs, often encountered in epilepsy as well, and in interpreting prognosis and etiology. However, the small number of participants in our study emerged as a limitation. Therefore, further studies using larger samples may enable the determination of a common etiology and thus the development of treatment and perhaps even preventative approaches.

References:

1. Brandt J, Seidman LJ, Kohl D. Personality characteristics of epileptic patients: a controlled study of generalized and temporal lobe cases. J Clin Exp Neuropsychol 1985;7(1):25-38.
2. Brodtkorb E, Mula M. Optimizing therapy of seizures in adult patients with psychiatric comorbidity. Neurology 2006;67(12 Suppl 4):S39-S44.
3. Barry JJ. The recognition and management of mood disorders as a comorbidity of epilepsy. Epilepsia 2003;44 (Suppl. 4):S30-S40.
4. Gilliam FG. Diagnosis and treatment of mood disorders in persons with epilepsy. Curr Opin Neurol 2005;18(2):129-33.
5. Harden CL, Goldstein MA. Mood disorders in patients with epilepsy: epidemiology and management. CNS Drugs 2002;16(5):291-302.
6. Akiskal HS, Placidi GF, Maremmani I, Signoretta S, Liguori A, Gervasi R, et al. TEMPS-I: delineating the most discriminant traits of the cyclothymic, depressive, hyperthymic and irritable temperaments in a nonpatient population. J Affect Disord 1998;51(1):7-19.
7. Akiskal HS, Rosenthal RH, Rosenthal TL, Kashgarian M, Khani MK, Puzantian VR. Differentiation of primary affective illness from situational, symptomatic, and secondary depressions. Arch Gen Psychiatry 1979;36(6):635-43.
8. Akiskal HS. Toward a temperament-based approach to depression: implications for neurobiologic research. Adv Biochem Psychopharmacol 1995;49:99-112.
9. Kochman FJ, Hantouche EG, Ferrari P, Lancrenon S, Bayart D, Akiskal HS. Cyclothymic temperament as a prospective predictor of bipolarity and suicidality in children and adolescents with major depressive disorder. J Affect Disord 2005;85(1-2):181-9.
10. Evans L, Akiskal HS, Keck PE, Jr., McElroy SL, Sadovnick AD, Remick RA, et al. Familiality of temperament in bipolar disorder: support for a genetic spectrum. J Affect Disord 2005;85(1-2):153-68.
11. Chiaroni P, Hantouche EG, Gouvernet J, Azorin JM, Akiskal HS. The cyclothymic temperament in healthy controls and familially at risk individuals for mood disorder: endophenotype for genetic studies? J Affect Disord 2005;85(1-2):135-45.
12. Rihmer Z, Akiskal KK, Rihmer A, Akiskal HS. Current research on affective temperaments. Curr Opin Psychiatry 2010;23(1):12-8.
13. Maina G, Salvi V, Rosso G, Bogetto F. Cyclothymic temperament and major depressive disorder: a study on Italian patients. J Affect Disord 121(3):199-203.
14. Cassano GB, Akiskal HS, Perugi G, Musetti L, Savino M. The importance of measures of affective temperaments in genetic studies of mood disorders. J Psychiatr Res 1992;26(4):257-68.
15. Coşar B. Cep Tıp Depresyon. Ankara: Bilimsel Tıp Yayınevi; 2005.
16. Köroğlu E. Mental Bozuklukların Tanısal ve Sayımsal Elkitabı (DSM-lV TR) (Amerikan Psikiyatri Birliği. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition). Dördüncü Baskı ed. Ankara: Hekimler Yayın Birliği; 2001.
17. Vahip S, Kesebir S, Alkan M, Yazici O, Akiskal KK, Akiskal HS. Affective temperaments in clinically-well subjects in Turkey: initial psychometric data on the TEMPS-A. J Affect Disord 2005;85 (1-2):113-25.
18. Chiaroni P, Hantouche EG, Gouvernet J, Azorin JM, Akiskal HS. Hyperthymic and depressive temperaments study in controls, as a function of their familial loading for mood disorders. Encephale 2004;30(6):509-15.

19. Lazary J, Gonda X, Benko A, Gacser M, Bagdy G. Association of depressive phenotype with affective family history is mediated by affective temperaments. Psychiatry Res 2009;168(2):145-52.

20. Gassab L, Mechri A, Bacha M, Gaddour N, Gaha L. Affective temperaments in the bipolar and unipolar disorders: distinctive profiles and relationship with clinical features. Encephale 2008;34(5):477-82.

21. Kanner AM. Epilepsy and mood disorders. Epilepsia. 2007;48 (Suppl. 9):S20-S2.

22. Mendez MF. Psychopathology in epilepsy: prevalence, phenomenology and management. Int J Psychiatry Med 1988;18(3):193-210.

23. Shamim S, Hasler G, Liew C, Sato S, Theodore WH. Temporal lobe epilepsy, depression, and hippocampal volume. Epilepsia 2009;50(5):1067-71.

24. Whittle S, Allen NB, Lubman DI, Yucel M. The neurobiological basis of temperament: towards a better understanding of psychopathology. Neurosci Biobehav Rev 2006;30(4):511-25.

25. Coan AC, Appenzeller S, Bonilha L, Li LM, Cendes F. Seizure frequency and lateralization affect progression of atrophy in temporal lobe epilepsy. Neurology 2009;73(11):834-42.

26. Noeker M, Haverkamp-Krois A, Haverkamp F. Development of mental health dysfunction in childhood epilepsy. Brain Dev 2005;27(1):5-16.