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Clinical Research

The Need For Subtypıng in Panic Disorder: A Cluster Analysis

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ABSTRACT

Objective: In this study, cluster analysis was performed with the data of various scales used in panic disorder patients. We aimed to make an effective subtyping in panic disorder that can affect the prognosis and treatment of the disease and also will be effective in the prevention of this disease.
Material and Method: A total of 110 panic disorder patients diagnosed with the DSM-5 Structured Clinical Interview-Clinical Version who met the inclusion criteria were included in this study. After the informed consent forms were obtained; Sociodemographic and Clinical Data Form, Panic and Agoraphobia Scale (PAS), Hamilton Depression Rating Scale (HAM-D), Hamilton Anxiety Rating Scale (HAM-A), Eysenck Personality Questionnaire Revised-Short Form (EPQR-S), Separation Anxiety Symptom Inventory, Anxiety Sensitivity Index-3 (ASI-3), and Childhood Trauma Questionnaire (CTQ) were applied to all participants. Univariate analysis, cluster analysis and discriminant analysis were performed with the collected data.
Results: As a result of multivariate analysis, we found two clusters in panic disorder. According to clustering characteristics, we identified 2 subtypes as traumatic panic disorder and nontraumatic panic disorder. Depression, anxiety levels, panic and agoraphobia scale, separation anxiety, anxiety sensitivity, neuroticism and psychoticism personality dimensions, childhood traumas, especially emotional abuse and sexual abuse, were found to be higher in the traumatic subtype. Eysenck extraversion personality dimension was higher in In the nontraumatic panic disorder subtype.
Conclusion: Characteristics in panic disorder patients are related to each other, and there are two subtypes: panic disorder that occurs with traumatic effect and Nontraumatic Panic Disorder.

Keywords: *Panic Disorder, Trauma, Panic Disorder Subtypes, Cluster Analysis.*

ÖZ

Panik Bozukluğunda Alt Tiplendirme İhtiyacı: Bir Küme Analizi
Amaç: Bu çalışmada panik bozukluğu hastalarında kullandığımız çeşitli ölçeklere ait verilerle küme analizi yapılmıştır. Panik bozukluğunda hastalığın prognozunu ve tedavisini etkileyebilecek, aynı zamanda bu hastalığın önlenmesinde de etkili olacak etkili bir alt tipleme yapmayı amaçladık.
Gereç ve Yöntem: Bu çalışmaya DSM-5 Yapılandırılmış Klinik Görüşmesi-Klinik Versiyonu ile tanı konan ve dahil edilme kriterlerini karşılayan toplam 110 panik bozukluğu hastası katılmıştır. Bilgilendirilmiş gönüllü onam formları alındıktan sonra; Sosyodemografik ve Klinik Veri Formu, Panik ve Agorafobi Ölçeği (PAS), Hamilton Depresyon Derecelendirme Ölçeği (HAM-D), Hamilton Anksiyete Derecelendirme Ölçeği (HAM-A), Eysenck Kişilik Anketi- Gözden Geçirilmiş Kısa Formu (EPQR-S), Ayrılma Anksiyetesi Belirti Envanteri, Anksiyete Duyarlılığı İndeksi-3 (ASI-3) ve Çocukluk Çağı Ruhsal Travma Ölçeği (CTQ) uygulanmıştır. Toplanan verilerle tek değişkenli analiz, küme analizi ve diskriminant analizi yapılmıştır.
Bulgular: Çok değişkenli analizler sonucunda panik bozukluğunda iki kümelenme olduğunu gördük. Kümelenme özelliklerine göre travmatik panik bozukluğu ve travmatik olmayan panik bozukluğu olmak üzere 2 alt tip belirledik. Travmatik alt tipte depresyon, kaygı düzeyleri, panik agorafobi ölçeği, ayrılma anksiyetesi, anksiyete duyarlılığı, nörotisizm ve psikotisizm kişilik boyutları, çocukluk çağı travmaları, özellikle duygusal istismar ve cinsel istismar daha yüksek bulunmuştur. Travmatik olmayan panik bozukluğu alt tipinde Eysenck dışadönüklük kişilik boyutu anlamlı yüksek olduğu saptanmıştır.
Sonuç: Panik bozukluğu hastalarında özellikler birbiriyle ilişkilidir ve travmatik etkiyle ortaya çıkan panik bozukluğu ve Travmatik Olmayan Panik Bozukluk olmak üzere iki alt tipi vardır.

Anahtar Sözcükler: *Panik Bozukluğu, Travma, Panik Bozukluğu Alt Tipleri, Küme Analizi.*

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Panic disorder manifests with sudden panic attacks, which generally occur in unexpected situations, giving a feeling of intense fear and discomfort. Anxiety about having panic attacks again after an attack leads to a significant decrease in quality of life and loss of functionality (1).

In recent years, the number of studies aiming to define subtypes of panic disorder has increased. In different studies, Starcevic et al. and Cox et al. (2, 3) made classifications based on symptoms. Massana et al. (4)

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examined the biological and psychological differences of panic disorder patients. Fidaner et al., Bovasso and Eaton (5, 6) made subtyping based on physical symptoms. There is a need for phenomenological re-evaluation for future classifications of panic disorders.
Cluster analysis is one of the multivariate statistical analysis methods that helps to separate units and variables into similar subsets (group, class) for groups that are not clearly known. The main goal of cluster analysis is to group units based on their characteristic features (7). Although there are panic disorder subtyping studies conducted in terms of symptoms, cluster analysis has not been yet performed. We planned to carry out this study with an analysis based on the characteristics of the symptoms. Determination of subtypes by cluster analysis will also contribute to studies on the prognosi and treatment of the disease. The objectives of this study were to determine the distribution of symptoms in panic disorder, to define the clinical features of the subtypes of the disease and the factors that determine this subtyping, and to define possible symptom clusters that can define the subtypes of the disease by cluster analysis method.

MATERIAL AND METHOD

This study was conducted in Manisa Celal Bayar University Health Sciences Hospital Psychiatry Clinic. The study protocol was approved by Manisa Celal Bayar University Medical Faculty, Non-Interventional Clinical Research Ethics Committee with the 01/06/2018 dated and 25558 numbered decision. The study sample consisted of 124 participants who presented to the psychiatry outpatient clinic of the hospital between June 2018 and February 2019 and were diagnosed with panic disorder through the DSM-5 Structured Clinical Interview (SCID 5) diagnostic evaluation interviews. Among these, 7 participants were excluded, because they aged over 65 years, 5 participants because they did not want to give written consent that they participated in the study, and 2 participants, because they could not receive the instructions and were unable to fill the forms. Written informed consent forms were obtained from the remaining 110 panic disorder patients.
All tests and scales were administered to the participants in this study by the same psychiatrist. The tests were placed in the test battery and the participants were asked to answer and fill them in a single session. The study type was determined as a cross-sectional and explanatory hierarchical cluster analysis. In the hierarchical clustering method, first it is assumed that there are n clusters first. As a first step, the two closest clusters are combined. In the second step, the renewed distance matrix is found by reducing the number of clusters by one. These two steps are repeated n-1 times. There are six different techniques based on this algorithm, including single correlation, full correlation, group mean, center, median and minimum variance techniques.
In the study, the number of clusters was determined as 2 using hierarchical methods. In our study, whether comorbidities, panic agoraphobia levels, depression degree, anxiety assessment, personality dimensions and characteristics, separation anxiety, anxiety sensitivity and childhood psychological traumas indicate a clustering was investigated in panic disorder patients. When we look at the clustering characteristics, one of them was determined as a panic disorder subtype developed with traumatic effect due to the high trauma characteristics, and the other was determined as a nontraumatic panic disorder subtype.
Inclusion criteria were being in the age range of 18-65, being diagnosed with panic disorder as a result of SCID 5 (DSM-5 Structured Clinical Interview), having the physical and mental capacity to fulfill the research instructions, accepting to participate in the study and to give written consent, in its current state, experiencing panic disorder symptoms actively and having had at least one panic attack in the last month. Exclusion criteria in the study were having delirium, dementia, or similar diagnosis and diagnosis groups in which the ability to evaluate is impaired, being under the age of 18 or over the age of 65 (since cognitive problems are more common and difficult to distinguish over the age of 65, and the necessity to obtain the consent of the guardian and the difficulty in establishing a clear diagnosis under the age of 18), having a chronic disease such as uremic encephalopathy, presence of alcohol and substance-related encephalopathy, and being under the influence of alcohol and substance, as well as being unable to complete the clinical interview and self-assessment scales in a healthy way.
After the informed consent forms were obtained; Structured Clinical Interview for DSM-5 (SCID-5CV), Sociodemographic and Clinical Data Form, Panic and Agoraphobia Scale (PAS), Hamilton Depression Rating Scale (HAM-D), Hamilton Anxiety Rating Scale (HAM-A), Eysenck Personality Questionnaire Revised-Short Form (EPQR-S), Anxiety Sensitivity Index-3 (ASI-3), Separation Anxiety Symptom Inventory (SASI), and Childhood Trauma Questionnaire (CTQ) were applied to all participants.
Structured Clinical Interview for DSM-5 (SCID-5CV): Structured Clinical Interview for DSM-5 Disorders was developed by First et al. The Turkish validity and reliability of the Structured Clinical Interview for DSM-5 Disorders was demonstrated in the study of Elbir M. et al. Psychiatric diagnoses were made by applying SCID-5 CV to our patients (8).
Panic and Agoraphobia Scale (PAS): It is used to rank severity in subsections by considering panic attacks, phobic avoidance, anticipatory anxiety, impairment in social relationships, and health concerns in patients. In a study conducted in Turkey, the highest specificity (92.94%) and sensitivity (92.00%) values are obtained with a cut-off value between 11-12

points. Turkish validity and reliability study was performed by Tural Ü et al. (9).

Hamilton Depression Rating Scale (HAM-D): It measures the level and severity of depression in the patient: 0-7 points no depression, 8-15 mild depression, 16-28 moderate depression, ≥ 29 severe depression. In the study conducted in Turkey, the cut-off score was calculated as 7. The Turkish validity and reliability study was performed by Akdemir A et al. (10).

Hamilton Anxiety Rating Scale (HAM-A): It is used to determine the anxiety level and symptom distribution to measure the change in anxiety severity of patients. It consists of 14 questions questioning both mental and physical symptoms. Turkish validity and reliability study was conducted by Yazici MK et al. (11).

Eysenck Personality Questionnaire Revised-Short Form (EPQR-S): Within the framework of Eysenck personality theory, it provides the evaluation and measurement of dimensions of personality such as neuroticism-stability, extroversion-introversion and psychoticism. Turkish validity and reliability study was made by Karancı AN et al. (12).

Anxiety Sensitivity Index-3 (ASI-3): It enables us to measure anxiety sensitivity with its physical, social and cognitive dimensions. It is a self-reporting scale. A high score indicates increased anxiety sensitivity. The Turkish validity and reliability study was performed by Mantar A et al. (13).

Separation Anxiety Symptom Inventory (SASI): This scale is an inventory that questions childhood separation anxiety symptoms in adults. The people who filled out the scale are asked to try to remember the fears they might have experienced when they were younger than 18 years old and fill in that period. The Turkish validity and reliability study was performed by Diriöz M et al. (14).

Childhood Trauma Questionnaire (CTQ): This scale is used to evaluate the experiences of abuse and neglect before the age of 20, retrospectively and quantitatively. It is a self-assessment scale, and patients are asked questions about the events they experienced before the age of 20, and to answer as truthfully as possible because it concerns their private lives. The Turkish validity and reliability study was performed by Şar V et al. (15).

Statistical Analysis

The analysis of the data in this study was made with the SPSS 15 program and studied with a confidence interval of 95%. Study data were evaluated by basic frequency analysis, followed by univariate analysis (Chi-square and Student's t test, ANOVA) and multivariate analysis by cluster analysis and discriminant analysis. Analysis assumptions were examined. Since the total number of subjects in the study was less than 300, the hierarchical (staged) clustering method was used as the clustering method. The "mean correlation between groups" method was used as the similarity method, and two clusters were formed in the resulting dendrogram.

When the clustering analysis was repeated with the k-means clustering technique, the clusters in which the cases were placed with the hierarchical method (2 clusters as nontraumatic panic disorder and the traumatic panic disorder) were reconstructed.

RESULTS

Of all participants, 70.9% (n =78) were female and 29.1% (n =32) were male patients. The mean age was 35±10 years, 24.5% of the patients were in the 25-34 age group, and 24.5% were in the 35-44 age group.

The income level of 68.2% of the participants was medium, 53.6% were married, and 33.6% were housewives. Of all patients included in the study, 30.0% experienced permanent loss of parents in their childhood (Table 1).

Table 1. *Distribution of demographic characteristics.*

		N (n :110)	Percentage (%)
Gender	Male	32	29.1
	Female	78	70.9
Age (years)	<25	18	16.4
	25-34	27	24.5
	35-44	27	24.5
	45-54	20	18.2
	> 54	18	16.4
Income	Poor	9	8.2
	Moderate	75	68.2
	Good	26	23.6
Marital status	Single	41	37.3
	Married	59	53.6
	Divorced/Separate	9	8.2
	Widow	1	0.9
Occupation	Unemployed	9	8.2
	Housewife	37	33.6
	Officer	18	16.4
	Worker	9	8.2
	Self-employed	6	5.5
	Farmer	1	0.9
	Retired	9	8.2
	Student	14	12.7
	Other	7	6.4
Parent loss in childhood	No	77	70.0
	Yes- (Death)	33	30.0
Place of living	Village	10	9.1
	County	26	23.6
	City	74	67.3
Place of growth	Village	23	20.9
	County	31	28.2
	City	56	50.9
Education Level	Literate	8	7.3
	Primary	31	28.2
	Middle	6	5.5
	High School	21	19.1
	University	44	40.0
Paternal Education Level	Illiterate	8	7.3
	Literate	12	1.,9
	Primary	46	41.8
	Middle	9	8.2
	High School	14	12.7
	University	21	19.1
Maternal Educa-tion Level	Illiterate	28	25.5
	Literate	7	6.4
	Primary	47	42.7
	Middle	11	10.0
	High School	7	6.4
	University	10	9.1

When the clinical characteristics of the patients in our study were examined; 47.3% of the patients had other anxiety disorders, 45.5% were using antidepressants actively and 51.8% were using antidepressants previously. A history of psychiatric treatment was found in 1st and 2nd degree relatives in 67.3% of the sample. The most common comorbidities in the study participants was major depressive disorder (31.8%), followed by agoraphobia (50.0%), and generalized anxiety disorder (20.0%).

As a result of the cluster analysis, 61 of the subjects were in the first cluster and 49 were in the second cluster. The 1st cluster was named as "the cluster formed by the traumatic effect" and the 2nd cluster as the "nontraumatic cluster".

Panic agoraphobia scale, Hamilton depression rating scale, Hamilton anxiety rating scale, Eysenck Personality Questionnaire neuroticism and psychoticism subscale total scores, separation anxiety symptom questionnaire total scores, anxiety sensitivity index scores, Childhood Trauma Questionnaire emotional abuse, physical abuse, physical neglect, emotional neglect and sexual abuse subscale scores were found to be higher in the first cluster. Table 2 shows the mean values of the scale variables in the clusters.

Table 2. *Distribution of mean statistics of scale variables by cluster.*

	Traumatic cluster (%)	Nontraumatic cluster (%)
PAS	41.23	30.88
HAM-D	29.77	13.86
HAM-A	41.30	23.71
EPQR-S-NEU	3.85	2.73
EPQR-S-EXT	3.03	4.08
EPQR-S-PSY	1.33	1.24
SASI	21.72	15.10
ASI-3	48.49	27.12
CTQ-EMO-ABU	9.89	8.10
CTQ-PHY-ABU	8.89	8.53
CTQ-PHY-NEG	8.85	9.02
CTQ-EMO-NEG	11.75	10.49
CTQ-SEX-ABU	7.10	5.84

PAS: *Panic and Agoraphobia Scale,* ***HAM-D:*** *Hamilton Depression Rating Scale,* ***HAM-A****: Hamilton Anxiety Rating Scale,* ***EPQR-S:*** *Eysenck Personality Questionnaire Revised-Short Form (****NEU: Neuroticism, EXT: Extraversion, PSY: Psychoticism****),* ***SASI:*** *Separation Anxiety Symptom Inventory,* ***ASI-3:*** *Anxiety Sensitivity Index-3,* ***CTQ:*** *Childhood Trauma Questionnaire (****EMO-ABU:*** *Emotional Abuse****, PHY-ABU:*** *Physical Abuse,* ***PHY- NEG:*** *Physical Neglect,* ***EMO-NEG:*** *Emotional Neglect,* ***SEX-ABU:*** *Sexual Neglect).*

**The participants were divided into two clusters using the Hierarchical Clustering Analyses method. When evaluated with the chi-square test, it was found that the CTQ-PHY-NEG and EPQR-S-EXT scores were higher in the non-traumatic cluster, while the remaining scores were higher in the traumatic cluster.*

In the ANOVA analysis performed to determine whether the variables differ in terms of clusters, the scales with significant differences between the groups are shown in table 3.

Table 3. *Significance of variables for clusters*.*

	Cluster		**Errors**		**F**	**p**
	Mean Square	**Degrees of freedom**	**Mean Square**	**Degrees of freedom**	**Mean Square**	**Degrees of freedom**
PAS	2911.911	1	47.297	108	61.567	0.000
HAM-D	6881.077	1	64.896	108	106.032	0.000
HAM-A	8398.666	1	56.988	108	147.376	0.000
EPQR-S-NEU	33.950	1	1.882	108	18.042	0.000
EPQR-S-EXT	29.892	1	4.515	108	6.621	0.011
EPQR-S-PSY	0.187	1	1.653	108	0.113	0.737
SASI	1190.566	1	71.600	108	16.628	0.000
ASI-3	12408.407	1	102.005	108	121.645	0.000
CTQ-EMO-ABU	86.404	1	18.506	108	4.669	0.033
CTQ-PHY-ABU	3.417	1	21.189	108	0.161	0.689
CTQ-PHY-NEG	0.766	1	13.210	108	0.058	0.810
CTQ-EMO-NEG	43.435	1	19.440	108	2.234	0.138
CTQ-SEX-ABU	43.251	1	10.982	108	3.938	0.050

PAS: *Panic and Agoraphobia Scale,* ***HAM-D:*** *Hamilton Depression Rating Scale,* ***HAM-A****: Hamilton Anxiety Rating Scale,* ***EPQR-S:*** *Eysenck Personality Questionnaire Revised-Short Form (****NEU: Neuroticism, EXT: Extraversion, PSY: Psychoticism****),* ***SASI:*** *Separation Anxiety Symptom Inventory,* ***ASI-3:*** *Anxiety Sensitivity Index-3,* ***CTQ:*** *Childhood Trauma Questionnaire (****EMO-ABU:*** *Emotional Abuse****, PHY-ABU:*** *Physical Abuse,* ***PHY- NEG:*** *Physical Neglect,* ***EMO-NEG:*** *Emotional Neglect,* ***SEX-ABU:*** *Sexual Neglect).*

**Anova.*

Accordingly; Panic and Agoraphobia Scale, Hamilton Depression Rating Scale, Hamilton Anxiety Rating Scale, Eysenck Personality Questionnaire Neuroticism and Extraversion subscales, Anxiety Sensitivity Index-3, Separation Anxiety Symptom Inventory, Childhood Trauma Questionnaire Emotional Abuse and Sexual Abuse subscales were found to be significant.

Table 4 shows that the mean scores of the scales included in the discriminant analysis were successful in separating the traumatic and non-traumatic groups.

Table 4. *The success of the mean scores of the scales included in the discriminant analysis in separating traumatic and non-traumatic groups*.*

Function	Eigenvalue	% of Variance	Cumulative %	Canonical Correlation
1	2.033(a)	100.0	100.0	0.819

**Discriminant analysis.*

(Canonical correlation 0.8192=0.67 and Eigen value >0.4).

Table 5 shows that mean group values are sufficient to provide discrimination (Wilks' Lambda: 0.33 and p <0.001).

Table 5. *Adequacy of average group values to ensure discrimination*.*

Test of Function(s)	Wilks' Lambda	Chi-square	df	P
1	.330	118.185	3	0.000

**Discriminant analysis.*

Table 6 shows which scale means are important in distinguishing between traumatic and nontraumatic groups.

Table 6. *The importance of scale averages in differentiating traumatic and non-traumatic situations.*

	Function Cluster Occurring with Effect of Traumas
HAM-D	0.908
HAM-A	0.804
PAS	0.305
EPQR-S-NEU	0.303
EPQR-S-EXT	-0.111
CTQ-PHY-ABU	-0.094
EPQR-S-(Negative Control)	-0.061
ASI-3	0.048
CTQ-EMO-NEG	-0.045
EPQR-S-PSY	-0.045
CTQ-TOTAL	-0.036
CTQ-SEX-ABU	-0.015
CTQ-EMO-ABU	0.007
CTQ-PHY-NEG	-0.006

PAS: *Panic and Agoraphobia Scale,* ***HAM-D:*** *Hamilton Depression Rating Scale,* ***HAM-A****: Hamilton Anxiety Rating Scale,* ***EPQR-S:*** *Eysenck Personality Questionnaire Revised-Short Form (****NEU: Neuroticism, EXT: Extraversion, PSY: Psychoticism****), **SASI:** Separation Anxiety Symptom Inventory,* ***ASI-3:*** *Anxiety Sensitivity Index-3,* ***CTQ:*** *Childhood Trauma Questionnaire (****EMO-ABU:*** *Emotional Abuse****, PHY-ABU:*** *Physical Abuse,* ***PHY- NEG:*** *Physical Neglect,* ***EMO-NEG:*** *Emotional Neglect,* ***SEX-ABU:*** *Sexual Neglect).*
*******Discriminant analysis.*

Accordingly; the Hamilton Depression Rating Scale and the Hamilton Anxiety Rating Scale were the most important scales and Panic - Agoraphobia Scale and Neuroticism subscale of the Eysenck Personality Questionnaire were the secondary scales in distinguishing between the groups.
Table 7 shows the classification results.

Table 7. *The classification results.*

pbcat			**Predicted group members**		**Total**
			traumatic	**nontraumatic**	**traumatic**
Original	Count (n)	Traumatic	55	3	58
		Nontraumatic	1	51	52
	%	Traumatic	94.8	5.2	100.0
		Nontraumatic	1.9	98.1	100.0
Cross Validation	Count (n)	Traumatic	54	4	58
		Nontraumatic	1	51	52
	%	Traumatic	93.1	6.9	100.0
		Nontraumatic	1.9	98.1	100.0

**Chi Square.*

Accordingly, 96.4% of the originally grouped cases and 95.5% of the cases grouped by cross-validation were correctly classified.

DISCUSSION

Upon analysis of the results of our study, it became evident that there are two distinct sub-clusters. The patients who participated in the study were divided into two groups based on the clustering of symptoms and scales, with one group comprising those with trauma-related symptoms and the other comprising those with symptoms unrelated to trauma. It was determined that 55.5% (n =61) of the patients were in the traumatic group (cluster 1) and 45.5% (n =49) were in the non-traumatic group (cluster 2). The Panic Agoraphobia Scale, Hamilton Depression Rating Scale (HAM-D), Hamilton Anxiety Rating Scale (HAM-A), Eysenck Personality Inventory neuroticism and extraversion subscales, Anxiety Sensitivity Index-3 (ASI-3), Separation Anxiety Symptom Inventory, and Childhood Trauma Questionnaire emotional abuse and sexual abuse subscales were identified as significant between the clusters. The HAM-D and HAM-A scales were identified as the most significant in differentiating between the clusters, while the Panic-Agoraphobia Scale and the neuroticism subscale of the Eysenck Personality Questionnaire were determined to be secondary scales.

It has been demonstrated that anxiety disorders, including panic disorder, are associated with a history of childhood sexual and physical trauma (16-18). While a history of trauma is not a prerequisite for the

development of panic disorder, a history of childhood trauma has been observed at a higher rate in clinical cases of panic disorder (17, 19).

A study conducted with 200 patients diagnosed with panic disorder revealed that individuals who experienced childhood abuse exhibited more severe panic disorder and agoraphobia, a higher prevalence of comorbid depression, and more adverse psychosocial experiences (21). In a study comprising 539 patients with panic disorder, it was reported that 54.5% of the patients had a history of childhood trauma (22). In our study, this rate was found to be 55.5%, exhibiting a course of development comparable to that observed in the existing literature. In a study conducted by Goodwin et al., it was demonstrated that the lifetime prevalence of numerous psychiatric disorders, including panic disorder and generalised anxiety disorder, increased markedly in individuals who had experienced abuse during childhood (17). The results of our study indicated that the subscales measuring sexual abuse and physical abuse were significantly higher in the traumatic subtype. A recent meta-analysis, which employed a similar methodology to our study, found that early physical abuse and sexual abuse experiences were risk factors for panic disorder. These findings suggest that a reduction in childhood traumas could potentially prevent a significant number of psychiatric disorders, including panic disorder.

In the course of our study, the majority of participants were women, and this was the case in both subtypes. However, the proportion of women was higher in the trauma-related panic disorder subtype (75.4%) than in the non-traumatic subtype (65.3%). A review of the literature reveals that women represent the majority of patients diagnosed with panic disorder. Similarly, as observed in our study, the majority of women with panic disorder had experienced childhood trauma (20, 22).

In our study, parental loss in childhood was observed with greater frequency in the trauma-related subtype (32.8%) than in the other subtype (26.5%). Prior research has demonstrated a correlation between parental loss or separation during childhood and the subsequent development of panic disorder in adulthood (23, 24). It can be posited that psychiatric issues experienced by children who have lost their parents in childhood can be averted by enhancing social support.

Furthermore, patients with panic disorder exhibit a higher prevalence of additional physical disorders, including metabolic syndrome and cardiovascular pathologies, compared to the general population (25, 26). Approximately half of the patients who participated in the study exhibited additional physical pathologies, particularly cardiovascular diseases.

The prevalence of depression was found to be significantly higher (51.8%) in the traumatic panic disorder subgroup. In a study investigating childhood traumas in panic disorder patients, a significantly higher rate of depression was observed in those with a history of trauma (21). In another study, the prevalence of emotional neglect, psychological and physical abuse in patients with anxiety and depression was found to be twofold higher than in control groups and approximately threefold higher in comorbid conditions (27). The presence of comorbid psychiatric disorders has been shown to have a detrimental impact on treatment response and compliance with treatment.

A study of the literature revealed that patients with panic disorder accompanied by major depressive disorder exhibited significantly higher rates of severe agoraphobia, nocturnal panic attacks, and a greater number of panic attacks in the previous month, in addition to a higher prevalence of social phobia (28). This indicates that comorbidities and treatment resistance may be more prevalent in individuals with a traumatic subtype, while treatment response may be less robust. It is widely accepted that early childhood losses constitute a risk factor for both panic disorder and depressive disorders. In a study conducted with 157 patients diagnosed with panic disorder, 34% of the participants reported a history of loss or separation in the early periods of their lives (before the age of 15) (29). The relationships between depressive disorders, panic disorder and traumatic experiences, comorbidities and other characteristics identified in the studies are parallel with those observed in our own study. It is important to consider these comorbidities when developing a treatment plan.

The neuroticism subscale of the Eysenck Personality Questionnaire was found to exhibit a statistically significant elevation in the traumatic panic disorder subgroup of patients included in the study. The neuroticism subscale of the Eysenck Personality Questionnaire examines reactivity or emotional consistency. It has been reported that patients with high scores on this subscale may exhibit low self-confidence, excessive emotionality, depressive features, anxious features, nervousness and shyness (30). In a study conducted with 70 patients diagnosed with panic disorder, a significant relationship was identified between trauma and neuroticism, with neuroticism being observed to be elevated in this group (31). In a study conducted with 314 patients with panic disorder, it was found that trauma was highly associated with neuroticism (32). Our findings align with those of previous studies, indicating that a higher neuroticism score in the traumatic panic disorder subtype is associated with anxiety and depression.

The extraversion subscale of the Eysenck Personality Questionnaire was found to exhibit a significantly higher mean score in individuals diagnosed with non-traumatic panic disorder compared to those diagnosed with other subtypes. Extraversion is a personality dimension that encompasses sociability, enjoyment of communication, sociability, and enjoyment of social interaction. Those who obtain high scores on this dimension are more likely to be sociable, to engage in joking behaviour and to have a larger number of friends. Therefore, the higher scores observed in the

non-traumatic subtype are a predictable finding and are consistent with the results of other studies.

The prevalence of separation anxiety was found to be statistically significantly higher in the subgroup of individuals with panic disorder that developed with a traumatic effect. Previous studies have demonstrated that individuals with a history of separation anxiety during childhood exhibit an elevated risk of developing panic disorder (33). Once more, childhood separation anxiety disorder has been identified as a significant risk factor for the development of various mental health disorders, particularly panic disorder and major depressive disorder (34).

The ADI-3 scores were found to be statistically significantly higher in the traumatic panic disorder subgroup. A substantial body of evidence has demonstrated that elevated anxiety sensitivity is associated with more intense and frequent panic attacks (35, 36). A correlation was identified between elevated ADI-3 physical sub-dimension scores and the presence of panic disorder in individuals who have experienced trauma.

The experience of trauma during childhood has been identified as a contributing factor in the development of anxiety sensitivity, which in turn represents a significant risk factor for the onset of panic disorder (37, 38). The markedly elevated prevalence of ADI-3 in the trauma-related PD subtype aligns with the existing literature. In light of these findings, it is imperative that childhood traumas be subjected to rigorous examination and treatment in order to prevent the development of psychiatric disorders in adulthood.

Upon examination of the clusters of panic disorder subtypes, it was found that the level of panic agoraphobia was statistically significantly higher in the traumatic panic disorder subtype. A study conducted in Turkey reported that the co-occurrence of panic disorder and agoraphobia was associated with a history of childhood sexual and physical abuse. Similarly, the same study revealed a strong correlation between childhood and adolescent traumas and the development of agoraphobia and suicidal tendencies (39).

A further statistically significant finding was that the level of anxiety was higher in the trauma-induced panic disorder subtype than in the non-traumatic panic disorder subtype. A substantial body of evidence indicates that exposure to traumatic experiences is associated with an increased risk of suicidal behaviour, more severe anxiety symptoms, depression and self-harm (40-42). The presence of trauma is associated with a heightened severity of anxiety symptoms in individuals diagnosed with panic disorder.

In our study, the prevalence of antidepressant use and combined psychiatric treatment was higher in patients with a trauma-related panic disorder subtype than in patients with a non-traumatic panic disorder subtype. It is postulated that the rate of receiving psychiatric treatment is higher in the trauma-related panic disorder subtype due to higher rates of anxiety sensitivity, separation anxiety, depression and trauma. As comorbidities are more common in this group, multidisciplinary clinical approaches may be appropriate in selected patients.

As a consequence, the Panic-Agoraphobia Scale, Hamilton Depression Rating Scale, Hamilton Anxiety Rating Scale, Eysenck Personality Questionnaire Neuroticism and Psychoticism dimension scores, Separation Anxiety and Anxiety Sensitivity Index, and Childhood Psychological Traumas Emotional Abuse, Emotional Neglect, Physical Abuse, and Sexual Abuse subscale scores were observed to be elevated in individuals diagnosed with traumatic panic disorder relative to those diagnosed with non-traumatic panic disorder.

Conclusion and Recommendations

The determination of panic disorder subtypes is of significant importance with regard to the course of the disease and the selection of appropriate treatment options. For this reason, studies aimed at subtyping have been conducted previously. However, our study is distinctive in that it is one of the few to examine the clustering of symptoms and personal characteristics of panic disorder patients and the relationship of these clusters with trauma.

In our study, we found that patients with traumatic panic disorder exhibited higher levels of depression and anxiety, separation anxiety, and anxiety sensitivity, as well as higher scores on neuroticism and psychoticism personality dimensions. Additionally, they reported a higher prevalence of childhood traumas, particularly emotional abuse and sexual abuse. In contrast, patients with non-traumatic panic disorder demonstrated higher levels of extroversion.

The findings of our study indicate that subtyping in panic disorder is essential for accurately assessing the severity of the disease, identifying medical and psychological comorbidities, evaluating the efficacy of pharmacological treatments, and differentiating between therapeutic responses. Given that the subtype of panic disorder caused by traumatic effects is more severe than the other subtype, with higher rates of comorbidities and resistance to treatment, it was hypothesised that the underlying traumatic issues should be addressed. It is therefore important to bear in mind that this subtype requires more intensive therapy, that follow-up examinations should be conducted at regular intervals, that comorbidities should be monitored closely and that organic diseases should be subject to rigorous surveillance. Furthermore, the findings of our study may prove useful in identifying risk groups in panic disorder and in guiding the implementation of appropriate measures.

It should be noted that this study is not without limitations. The sample size is relatively limited. A larger sample size will facilitate the identification of more distinct clusters and the discovery of additional clusters. It will thus become evident that certain characteristics, which are not deemed statistically significant, are in fact significant. Furthermore, due to the extensive number of scales utilized in the study,

each patient was allotted an hour to complete the assessments. While completing the scales, patients occasionally expressed boredom and encountered difficulties, which may have resulted in distraction. Some patients indicated a preference for not self-reporting and reported difficulty in understanding the scales. Finally, medication use was not restricted in our panic disorder patients, as it was thought that medication use might negatively affect some scale scores, particularly those related to panic-agoraphobia.

In conclusion, the existing literature on panic disorder is relatively limited with regard to studies investigating all of the aforementioned characteristics in terms of panic disorder and determining subtypes by cluster analysis. Furthermore, additional studies with a larger number of patients are required in order to investigate other potential clusters.

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