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Research / Araştırma

Evaluating The Subtypes of Panic Disorder by using Principal Component Analysis

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ABSTRACT

Evaluating the subtypes of panic disorder by using principal component analysis

Objective: Panic disorder is put forward to have a heterogeneous structure and multiple subtypes. Evaluating the different subtypes is important for diagnosis, treatment and prognosis. Studies about the quantitative psychopathology assessment are so rare. We aim to determine the subtypes with principal component analysis of panic attack symptoms.

Method: 159 outpatients with panic disorder who had referred to the anxiety disorder outpatient unit in Bakirkoy Research and Training Hospital for Psychiatry, Neurology and Neurosurgery were included in the study. A sociodemographic questionnaire that was prepared by the investigators, The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I), Panic and Agoraphobia Scale (PAS), Hamilton Depression Rating Scale (HAM-D), Beck Anxiety Inventory (BAI) were used in the study. Variables with 15 items were created adding 'Fear of stroke' and 'desire to escape, restlessness'. Principal Component Analysis was applied according to the panic symptoms that the patiens declared.

Results: Six loading factors were obtained explaning 56% of total variance in Principal Component Analysis. The first set was named autonomic activation, the second was vestibular symptoms, the third was cardiovascular symptoms, the fourth was pseudoneurologic symptoms, the fifth was respiratory system symptoms and the sixth was fear of death.

Conclusion: Symptom profiles in our study were compatible with DSM-IV-TR diagnostic criteria. Significant panic disorder subtypes were found in principal component analysis.

Key words: Panic attack symptoms, panic disorder, subtypes by symptoms principal component analysis

ÖZET

Ana bileşenler analizi ile panik bozukluğu alt tiplerinin değerlendirilmesi

Amaç: Panik bozukluğunun (PB) değişik alt tiplerinin olduğu ve farklı alt tiplerin belirlenmesinin tanı, tedavi ve sonlanım açısından önemli olduğu ileri sürülmektedir. PB'nin psikopatolojisinin kantitatif değerlendirilmesi konusundaki çalışmalar azdır. Çalışmamızda, panik atak belirtilerinin faktör analizine dayanan alt tiplerinin belirlenmesi amaçlanmıştır.

Yöntem: Çalışmamız, Bakırköy Prof. Dr. Mazhar Osman Ruh Sağlığı ve Sinir Hastalıkları Eğitim ve Araştırma Hastanesi ikinci basamak polikliniklerine başvuran ve çalışmaya dahil edilme ölçütlerini karşılayan 159 hasta üzerinde gerçekleştirildi. Çalışmada, araştırıcılar tarafından hazırlanan sosyodemografik bilgi formu, DSM-IV Eksen I Bozukluklar İçin Yapılandırılmış Klinik Görüşme Formu (SCID-I), Panik Agorafobi Ölçeği (PAÖ), Hamilton Depresyon Derecelendirme Ölçeği (HAM-D), Beck Anksiyete Ölçeği (BAÖ) kullanıldı. DSM IV-TR panik atak tanı ölçütlerinde bulunan 13 maddeye, "felç olma korkusu" ile "kaçma isteği, yerinde duramama hali"nin eklenmesiyle toplam 15 maddeden oluşan değişkenlere, katılımcıların son panik ataklarında yaşadıklarını bildirdikleri belirtilere göre Ana Bileşenler Analizi uygulandı.

Bulgular: Ana Bileşenler Analizinde toplam varyansın %56'sını açıklayan 6 ayrık faktör kümesi elde edildi. Birinci küme otonomik aktivasyon kümesi, ikinci küme vestibüler belirtiler, üçüncü küme kardiovasküler belirtiler, dördüncü küme psödonörolojik belirtiler, beşinci küme solunum sistemi belirtileri ve altıncı küme ölüm korkusu kümesi olarak adlandırıldı.

Sonuç: Çalışmamızda elde edilen belirti profilleri DSM-IV-TR tanı ölçütlerini desteklemektedir. Ana Bileşenler Analizinde, varyansın önemli bir kısmını açıklayan anlamlı alt tipler oluşmuştur.

Anahtar kelimeler: Panik atak semptomları, panik bozukluğu, ana bileşenler analizi ile alt tipler

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INTRODUCTION

One year prevalence of panic disorder (PD) is 2.1% and lifetime prevalence is 5.1% in United States of America. One year and lifetime prevalence of agoraphobia are 0.6% and 1.1%, respectively (1). Panic attack is described as abrupt beginning of 4 of 13 symptoms listed in DSM-IV-TR and a period of intense fear and distress (2). PD is a variable disorder in terms of physical, physiological and cognitive symptoms of panic attack. It has been suggested that, since there are panic attacks consisting of very different symptom clusters, there may be subtypes of this disorder and that failure to distinguish these subtypes may lead to theoretical, methodical and treatment errors (3). For these reasons, subtyping studies based on factor analysis of symptoms during panic attacks have been conducted (4-8).

Several features have been taken into account in order to detect subtypes of PD. Presence of agoraphobia (9), nocturnal panic attacks (10), prominent symptoms during panic attacks (11,12), timing of panic attacks (13,14), biological features of the disorder (15), genetic liability (16) are among these features.

PD has been subtyped into different groups, regarding prominent panic attack symptoms as PD with heart and pulmonary symptoms (17), vestibular symptoms (18), gastrointestinal symptoms (19), depersonalization/derealization (20) or without subjective sense of fear (21).

Starcevic et al. (9) divided panic attack symptoms as more important (first rank) and those with secondary importance (second rank). First rank symptoms include; palpitations, tachycardia, dyspnea, dizziness or feeling faintness and trembling. Second rank symptoms are choking, shortness of breath, chest pain, numbness, hot flashes, depersonalization/derealization and nausea. Studies in this field have reported that the broadest part of the variance is explained by cardiorespiratory and vestibular factors (8,22-24).

In the literature, other groups detected with factor analysis are cognitive symptoms, depersonalization, numbness and autonomic activation. It has been argued that this clinical heterogeneity may have important implications on etiology, course and treatment of the disorder (3).

In the literature, when compared to other psychiatric disorders, there are fewer studies which investigated quantitative evaluation of PD psychopathology. Segui et al. (5) using factor analysis, found four factors among panic attack symptoms; cardiorespiratory, vestibular, mixed symptoms and general arousal. The authors also reported that factor analysis is a very valuable method to study subtyping and that more studies are necessary on this issue.

In our study, our aim was to detect subtypes of PD, based on factor analysis, in our country.

METHOD

Sample

159 consecutive patients who applied to Bakirkoy Training and Research Hospital for Psychiatry, Neurology and Neurosurgery secondary care outpatient clinics and who volunteered to participate to the study were included. Thirty-two patients did not accept to participate in the study. Seventeen patients were excluded since they did not fulfill inclusion criteria. Inclusion criteria were; at least having panic attack during the last month, being 18-64 years of age, PD disorder per DSM IV-TR diagnostic criteria (2) and having necessary cognitive abilities to fill self-report forms in the study. Exclusion criteria was having PD diagnosis associated with general medical condition or direct physiological effects of alcohol/substance per DSM IV-TR diagnostic criteria.

PD diagnosis were validated and comorbid conditions, particularly agoraphobia, were evaluated by the researchers by using Structural Clinical Interview for DSM IV Axis I Disorders (SCID-I) since original diagnosis of the patients were made by clinicians who were not included in the study. Tests in the test battery were administered in a random order during a single session. Ethical board approval from Bakirkoy Training and Research Hospital for Psychiatry, Neurology and Neurosurgery instutional review board before the

study. Sociodemographical data of the study are formerly used in another study, "Panic disorder and comorbidity" (25).

Measures

Sociodemographical Data Form: The form is developed by the researchers, by adding factors which can influence etiology and course of PD to sociodemographical data form provided in SCID-I interview manual. Besides, we detected symptoms experienced by the patients during their latest panic attacks, by adding symptoms which are thought to be features of panic attack and which have been frequently stated by our patients during our clinical practice, such as "fear of paralysis" (5) and the symptom, "restlessness, need to escape", which was suggested to be included in DSM diagnostic criteria by Cox et al. (26).

Structural Clinical Interview for DSM IV Axis I Disorders (SCID-I): It is a structured clinical interview to evaluate Axis I disorders by First et al. (27). SCID-I was adapted to Turkish by Corapcioglu et al. (28). SCID-I detects lifetime presence of axis one disorders.

Panic Agoraphobia Scale (PAS): It is developed by Bandelow et al. (29). There are clinical observer and patient self-report forms. It can be applied to PD patients regardless of the presence of agoraphobia. There are five subscales.

A- Features of panic attack: Three items are rated and one item is unrated,

B-Agoraphobia and avoidance behavior: Three items,

C-Anticipatory anxiety: Two items,

D-Disability: Three items,

E- Worries about health: Two items.

Each subscale score is computed by adding item scores in that particular subscale and total score is obtained by summing all items. It is adapted to Turkish by Tural et al. (30).

Hamilton Rating Scale for Depression (HAM-D): It is a 17-items scale, developed by Williams et al. (31) to evaluate the level and change of severity of depression. It is adapted to Turkish by Akdemir et al. (32).

Beck Anxiety Inventory (BAI): It is a 17-items scale, developed by Beck et al. (33) to measure the severity of anxiety experienced by the individual. Higher scores correspond to increased levels of anxiety. The scale is adapted to Turkish by Ulusoy et al. (34).

Statistical Analysis

Principal Component Analysis were computed on the variables including 15 items; 13 items in DSM IV-TR panic attack diagnostic criteria and 2 additional items which were reflecting the experiences of the patients in their last panic attack. Common factors were computed by using ortogonal factor model on the detected principal components. After this, factor loadings and weight of each item on the factor were computed by applying Varimax rotation. Factors with eigenvalues higher than 1 are included in the analysis. Pearson chi-square test is used to compare categorical variables. $p<0.05$ was accepted as statistically significant. Statistical analysis were computed with SPSS for Windows 11.0 software.

RESULTS

Hundred twenty of the participants were women (75.5%), and 39 were men (24.5%). Mean age of the participants was 39.16±11.24 years. Sociodemographical features of the patients were summarized in Table 1 and scale scores were summarized in Table 2. Symptoms of the last panic attack experienced by the participants were shown in Table 3. Principal Components Analysis revealed 6 factors with eigenvalues larger than 1, which explained 55.94% of the variance, cumulatively (Table 4).

First factor (variance=15%) consisted of symptom cluster hot flushes or chills, sweating, loose of control and nausea or stomach ache, these last two were

Table 1: Sociodemographical features

	n (%)
Gender	
Female	120 (75.5)
Male	39 (24.5)
Married	118 (74.2)
Marital status	
Single	25 (15.7)
Widow/divorced	16 (10.1)
Education	
First grade	93 (58.4)
Second grade-highschool	55 (34.5)
College	11 (6.9)
Employment	
Unemployed	6 (3.8)
Civil servant/self employed	150 (94.3)
Student	3 (1.8)
Medical disorders accompanying PD	35 (22.0)
Agoraphobia	108 (67.9)
	Ort±SD
Age (years)	39.16±11.24
PD age of onset (years)	33.30±10.81
PD duration (years)	5.96±6.05
Time to diagnose PD (years)	1.67±4.00
Time to apply for psychiatric treatment (years)	4.47±4.62
Duration of PD treatment (years)	4.40±4.63

PD: Panic Disorder

Table 2: Scores obtained from the scales

	Mean±SD
Ham D	6.01±4.64
BAS	17.67±12.50
PAS total	13.04±9.68
PAS-A	2.80±3.08
PAS-B	3.47±3.71
PAS-C	3.68±2.06
PAS-D	2.04±2.61
PAS-E	1.06±1.37

Ham D: Hamilton Rating Scale for Depression, BAS: Beck Anxiety Scale, PAS: Panic Agoraphobia Scale

distributed to first, fifth and sixth factors by borderline values. Second factor (variance=9.38%) included dizziness, lightheadness feelling faint, trembling or shaking, and depersonelization/derealization symptom cluster. Third factor (variance=8.89%) included palpitations, tachycardia or perception of heartbeats, chest pain and discomfort symptom cluster. Fourth factor (variance=7.95%) consisted of numbness/tingling, fear of paralysis, and dyspnea and sensation of being smothered, which were mainly loaded in the fifth factor. Fifth factor (variance=7.5%) included dyspnea or sensation of being smothered, choking and fear of loosing control or going insane, which were mainly loaded in the first factor, and nausea or stomach pain, which were distributed to three factors. Sixth factor (variance=7.1%) consisted of fear of dying, need to escape, restlessness and nausea or stomach ache symptoms (Table 4).

Table 3: Profile of panic attack symptoms (n=159)

Symptoms	Total (%)
Palpitations, tachycardia	91.2
Fear of dying	87.4
Numbness/tingling	76.7
Shortness of breath or sensation of being smothered	76.7
Dizziness, faintness	75.5
Shaking/trembling	74.2
Chest pain or discomfort	73.6
Chills or hot flushes	73.6
Sense of choking	69.1
Sweating	67.3
Fear of loosing control or going insane	66.0
Nausea, stomachache	49.1
Depersonalization or derealization	31.4
Fear of paralysis	42.8
Need to escape, restlessness	71.1

DISCUSSION

In their study on phobic avoidance, Turgeon et al. (35) found a significant difference between women and men only in phobic avoidance and there were no significant gender differences in the other components of agoraphobia. In our study, while there was a gender difference in the rate of agoraphobia, this was not statistically significant.

When compared with other psychiatric disorders, subtyping studies, based on symptom profile, by using factor analysis is less common in PD. Using DSM-IV-TR panic attack diagnostic criteria in their phenomenological study, Segui et al. (5) found 4 groups which explained 57% of the total variance. The biggest group explained 26.1% of the total variance,

Table 4: Results of principal components analysis (n=159)

Symptoms	Autonomic 15%	Vestibular 9.38%	Cardiovascular 8.89%	Pseudoneurological 7.95%	Respiratory 7.5%	Fear of dying 7.1%
Palpitations, tachycardia			0.547			
Fear of dying						0.589
Numbness/tingling				0.524		
Shortness of breath or sensation of being smothered				0.270	0.526	
Dizziness, faintness		0.496				
Shaking/trembling		0.434				
Chest pain or discomfort			0.487			
Chills or hot flushes	0.448					
Sense of choking					0.563	
Sweating	0.428					
Fear of loosing control or going insane	0.392				0.224	
Nausea, stomachache	0.207				0.244	0.249
Depersonalization or derealization		0.429				
Fear of paralysis				0.413		
Need to escape, restlessness						0.561

cardiorespiratory symptoms factor, and included chest pain, palpitation, numbness, dyspnea and shaking, trembling and fear of dying. The second factor explained 15.1% of the total variance, vestibular symptoms factor, and consisted of dizziness, faintness, fear of loosing control and going insane. The third factor explained 8.5% of the total variance, mixed symptoms factor, and included symptoms such as sweating, depersonalization/derealization, sensation of smothering and hot flushes. The fourth and last factor explained 7.2% of the total variance, general arousal symptoms factor, and included gastrointestinal symptoms (stomachache, nausea, vomiting), shaking, trembling, hot flushes and numbness. Factor with these high variance rates suggested that PD was not a homogeneous group and might involve subtypes.

In a similar study, Briggs et al. (7) used Principal Components Analysis and found five factor, which explained 49% of the total variance. Among these factors, two factors in which respiratory symptoms were dominant or not were significant. There were no significant differences between these groups in terms of sociodemographical variables, only symptom profiles were significantly different. Phenomenological and treatment comparisons revealed that spontaneous panic attacks were more common in patients with respiratory complaints and that this group responded to imipramine better. Situational panic attacks were more common in the group without respiratory complaints and they responded better to alprozolam. Authors claimed that symptom based subtyping might predict treatment response.

Shioiri et al. (36) added "agoraphobia" and "anticipatory anxiety" to the 13 DSM-III-R panic attack criteria and studied these 15 items in 247 patients. They compared panic attacks with panic attacks with restricted symptoms in cluster analysis. There were 3 clusters in the panic attack group and 4 clusters in the restricted symptom attack group. They found that there were differences between the groups in terms of symptom distribution and frequency, thus, attacks with restricted symptom represent a different group than panic attacks.

Cox et al. (26) added "hopelessness" and "restlessness, need to escape" to the 13 items included in DSM-III-R panic attack criteria and studied these 15 items in 212 patients. Principal Components Analysis revealed three factors. First factor included mainly symptoms associated with dizziness, second factor included mainly cardiorespiratory symptoms and the third factor included mainly cognitive symptoms. Authors stated that PD was a heterogenous disorder and that DSM diagnostic classification was limited.

In our study, we conducted Principal Components Analysis with the 15 variables, that was formed up by adding two items which have been frequently stated by our patients during our clinical practice, (5) to DSM-IV-TR panic attack diagnostic criteria; "fear of paralysis", which is thought to be a feature of panic attack and and the"restlessness, need to escape" symptom which was suggested to be included in DSM diagnostic criteria by Cox et al. (26). Six factors explained 55.94% of the total variance. These factors were labeled as autonomic hyperactivity, vestibular, cardiovascular, pseudoneurological, respiratory and fear of dying groups, based on the loaded items.

First group, labeled autonomic hyperactivity consisted of symptom cluster hot flushes or chills, sweating, loose of control and nausea or stomach ache, which were closer to lower limit. Second group which was labeled as vestibular, included dizziness, lightheadness feelling faint, trembling or shaking, and depersonelization/derealization symptom cluster. Third group was labeled as cardiovascular group and included palpitations, tachycardia or perception of heartbeats, chest pain and discomfort symptom cluster. Fourth group consisted of pseudoneurological symptoms, such as numbness/tingling, fear of paralysis, and dyspnea and sensation of being smothered. We belive that numbness triggered fear of paralysis and formed this factor. Fifth group (variance=7.5%) included dyspnea or sensation of being smothered, choking and fear of loosing control, nausea or stomach pain, which were closer to lower limit. This group was labeled as respiratory group. The sixth and last group consisted of fear of dying, need to escape, restlessness and associated borderline symptoms of nausea or stomach ache. This group was labeled as fear of dying group since the main loading was on this fear.

There were some limitations of the present study. Having a medical disorder comorbid with PD may have an effect on panic symptoms. Although having PD due to general medical conditions was an exclusion criteria in our study, we did not specifically investigate medical disorders which could be associated with PD. We did not evaluate axis II comorbidities by SCID-II. Therefore, we did not evaluate whether patients had pure panic disorder. Since this was a retrsopective study, other limitations included exaggeration and difficulties in remembering the symptoms.

Results of our study indicated that there were very significant phenomenological subgroups among panic attack symptoms, which were based on Principal Components Analysis, a very important method to make this evaluation. The subgroups in our country seemed to be consistent with subgroups reported from other studies. Detecting panic disorder subtypes may help to predict treatment variablity, treatment response and selection of treatment in resistant cases. Subtyping via investigation of symptom structure variability may also set an example for other anxiety disorders.

Limitation of the study is lack of examining the possible effects of DSM-IV TR axis II disorders, since these disorders were not excluded. New studies which assess axis II disorders may yield important results.

In conclusion, results indicated that PD symptoms in our patients supported DSM-IV-TR diagnostic criteria and that quantitative methods differentiates PD into meaningful subgroups in a natural setting. DSM diagnostic system describes 13 symptoms associated with panic attack and implies that at least four of these symptoms must occur simultaneously. Physical and psychological symptoms in this broad spectrum are seen in certain loadings in most of the patients and presence of one symtpom seems to be a predictor of another symptom. This variable grouping may guide the researcher and clinician to form the treatment of therapy of the disorder, which also shows a variability in treatment response.

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