

Possible Subtypes of Panic Disorder

Arzu SARP¹, Ali Cezmi ARIK², Hatice GÜZ³, Ahmet Rifat ŞAHİN⁴, Zuhâl ABANOZ⁵

Abstract

Objective: The present study, is aimed to investigate the distribution and dispersion of panic attack symptoms, the possible subtypes of panic disorder, and the clinical features related to these subtypes in patients with panic disorder.

Material and Methods: The study included 105 patients that presented to the Ondokuz Mayıs University Faculty of Medicine Psychiatric Outpatient Clinic and met the DSM-IV-TR diagnostic criteria for panic disorder. The Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID-I), Panic Attack Symptom Checklist (PASC), Structured Clinical Interview for DSM-III-R (SCID-II), Beck Anxiety Inventory (BAI), Anxiety Sensitivity Index (ASI), Panic Disorder Severity Scale (PDSS), and Panic and Agoraphobia Scale (PAS) were administered to all the patients. This study examined the correlation between clinical scales and the factors based on factor analysis using PASC.

Results: The 3 most frequently observed symptoms during panic attacks were palpitation, sensations of shortness of breath, and sensation of choking, and the 3 most severe were palpitation, chest pain, and sensation of shortness of breath. The 3 most frequently observed non-DSM-IV-TR symptoms were feeling of discomfort, dry mouth, and blurred vision. As a result of our analysis, 3 factors were defined: respiratory-circulatory, cognitive, and autonomic. Panic attack severity, panic attack frequency, and grade of agoraphobia were strong predictors of the respiratory-circulatory subtype; anticipatory anxiety was a strong predictor of the cognitive subtype. Grade of being anxious for health was stronger predictor for respiratory-circulatory subtype, predictor for the "autonomic" subtype, and a reverse predictor for the cognitive subtype.

Conclusion: It should be considered that the panic attack symptoms in DSM-IV-TR are insufficient to determine the panic disorder subtypes that are based on symptom profiles. The determination of subtypes could contribute in prognosis of disorder and studies about treatment methods.

Key Words: Panic disorder, subtypes, factor analysis

INTRODUCTION

Panic disorder (PD) is defined in DSM-IV-TR, as a disorder characterized by the unexpected and recurrent panic attacks accompanied with at least 4 of 13 somatic or cognitive symptoms. In the recent years, the research that focused on the symptom clusters and the subtypes of panic disorder has offered different definitions.

The studies that used biological parameters to identify the subtypes of PD determined the characteristics

that distinguished cardiorespiratory from gastrointestinal (Lelliot et al., 1990), respiratory from non-respiratory (Briggs et al., 1993; Biber et al., 1999), and respiratory from cognitive subtypes (Moynihan and Gevirtz, 2001). There are some studies, which topographically classified the subtypes according to the body part as *cephalo-vertiginous*, *cervico-respiratory*, *thoracic cardiac*, and *abdomino-digestive* (Pio-Abreu et al., 1998). Mas-sana and colleagues (2001) divided PD patients into two groups according to the cardio-respiratory and pseudo-

Received: 03.11.2009 - Accepted: 12.03.2010

¹Specialist, Muş State Hospital, Division of Psychiatry, Muş ²Prof., ³Prof., ⁴Prof., Department of Psychiatry, Ondokuz Mayıs University, Faculty of Medicine, Samsun, ⁵Specialist, Batman State Hospital, Division of Psychiatry, Batman.

Arzu Sarp MD., e-mail: arzusarp@gmail.com

TABLE 1. Frequency and severity of Panic Attack symptoms.

DSM-IV-TR symptoms	number	%	severity mean $\pm$ ss
Palpitation	105	100	1.97 $\pm$ 0.80
Shortness of breath	94	89.5	1.69 $\pm$ 0.93
Feeling of choking	93	88.6	1.60 $\pm$ 0.90
Dizziness /drowsiness	92	87.6	1.44 $\pm$ 0.90
Fear of death	87	82.9	1.62 $\pm$ 1.01
Chest pain/discomfort	84	80.0	1.69 $\pm$ 1.11
Paresthesia	78	74.3	1.22 $\pm$ 0.93
Feeling cold/hot	78	74.3	1.07 $\pm$ 0.85
Depersonalization/derealization	76	72.3	1.12 $\pm$ 0.96
Nausea/abdominal pain	75	71.4	1.04 $\pm$ 0.85
Shivering/shaking	73	69.5	1.03 $\pm$ 0.88
Fear of going mad/loosing control	72	68.6	1.05 $\pm$ 0.93
Perspiration	60	57.1	0.93 $\pm$ 0.89
Symptoms not present in DSM-IV-TR			
Discomfort	89	84.8	1.45 $\pm$ 0.89
Dryness of mouth	76	72.4	1.40 $\pm$ 1.09
Blurry vision	72	68.6	1.06 $\pm$ 0.89
Feeling of strangulation in the throat	71	67.6	1.19 $\pm$ 1.03
Desperation/hopelessness	66	62.9	0.81 $\pm$ 0.78
Difficulty to focus	47	44.8	0.63 $\pm$ 0.83
Blurry mind	42	40.0	0.59 $\pm$ 0.82

neurologic symptoms. At the end of the lactate provocation test, the researchers determined tachycardia and perspiration symptoms in the group that showed cardio-respiratory symptoms, whereas they found bradycardia and extensive perspiration symptoms in the group that showed pseudo-neurological symptoms. The presence of a symptom that appears without “fear of death” or “fear of going mad or losing control” has been discussed (Rus-sel et al., 1991). The studies conducted with the patients who had chest pain revealed evidence supporting the presence of “panic disorder in the absence of fear” (Fleet et al., 2000; Bringager et al., 2008).

Cox and colleagues (1994) classified the panic disorder symptoms, whether they were included in DSM III-R or not, into the subtypes “dizziness”, “cardio-respiratory”, and “cognitive” using factor analysis.

Despite the presence of other subtypes, the majority of the studies examined the respiratory subtype. Briggs and colleagues (1993) defined the respiratory subtype with the presence of at least 4 symptoms of shortness of breath, feeling of choking, fear of death, chest pain, and paresthesia. The fact that the respiratory subtype was shown to be more sensitive to the CO₂ provocation test in a number of studies is the most important supportive

evidence for the presence of the respiratory subtype. The respiratory subtype definition of Briggs and colleagues has been accepted as a criterion to identify the subtype in the studies that used biological parameters (Freire et al., 2008; Valenca et al., 2002; Abrams et al., 2006; Nardi et al., 2006).

Biber and Alkin (1999) defined the respiratory subtype according to the increased response to 35% CO₂ inhalation, whereas Hegel and Ferguson (1997) defined this subtype according to the low pCO₂ values in patients. The respiratory subtype was found to be related to the increased sensitivity to 35% CO₂, extended duration of the disorder, the experience of a traumatic asphyxia and the history of a respiratory illness, and heavy smoking (Verburg et al., 1995; Bouwer and Stein, 1997; Biber and Alkin, 1999; Valenca et al., 2002). A study conducted in Turkey revealed high levels of anxiety sensitiveness and high total scores on Panic and Agoraphobia Scale (PAS) in the patients determined according to the respiratory subtype definition of Briggs and colleagues (1993) (Onur et al., 2006a). In addition to that, some studies showed that agoraphobia was more severe in the respiratory subtype (Briggs et al., 1993; Nardi et al., 2004; Telch et al., 2003). The nocturnal panic attacks have been also found to be related to the respiratory subtype in some of the studies (Freire et al., 2007; Sarisoy et al., 2008).

Another subtypes defined as the depersonalization and derealization subtype was shown to appear at early ages and to have more severe prognosis. Additionally, this subtype was found to be related to increased avoidance behavior and number of attacks (Cassano et al., 1989; Segui et al., 2000a; Marquez et al., 2001). Some studies pointed to the presence of PD subtypes that had an early and late age at onset (Segui et al., 1999; Goodwin et al., 2002). Although the severity and family history of the disorder was found to be low in patients with late onset, the frequency of having affective disorder, particularly the dysthymic disorder was high (Segui et al., 2000b). A family study provided evidence for another subtype related to the increased familial risk accompanied by the choking symptoms (Horwatt et al., 1997). PD symptoms may also display gender differences. In a study, it was reported that the respiratory symptoms were identified more in female patients (Sheikh et al., 2002).

As a result, the studies which focused on this subject showed that the panic symptoms were generally classified in five groups; respiratory, nocturnal, fearless, cognitive, and vestibular (Kircanski et al., 2008).

TABLE 2. Rotated factor matrix (Varimax method).

Symptoms of panic disorder	Factor 1. Respiratory-circulatory	Factor 2. Cognitive	Factor 3. Autonomic
Symptoms present in DSM-IV-TR			
Palpitation	.767		
Perspiration			.405
Shivering/Shaking			.756
Nausea/abdominal pain			.780
Dizziness/drowsiness			.773
Depersonalization/derealization		.841	
Fear of going mad/loosing control		.829	
Feeling cold/hot			.589
Shortness of breath	.783		
Feeling of choking	.803		
Chest pain/discomfort	.713		
Fear of death	.774		
Paresthesia	.786		
Symptoms not present in DSM-IV-TR			
Blurry vision	.797		
Dryness of mouth	.830		
Discomfort		.753	
Difficulty to focus		.845	
Blurry mind		.798	
Desperation/Hopelessness		.700	
Feeling of strangulation in the throat	.748		
% variance	34.31	16.55	10.88
Eigen value	6.86	3.31	2.17

Note: (the values whose correlation coefficient 0.40 and over were presented here).

It is claimed that several factors such as severity and prognosis of the disorder, psychiatric and physical comorbid disorders, and response to treatment would be important in determining the subtypes of PD. The present study aimed to investigate the distribution of panic attack symptoms, the possible subtypes of panic disorder, the clinical features related to these subtypes and the significant factors that determined these subtypes in a group of patients with panic disorder.

MATERIAL AND METHOD

The present study was conducted with 105 patients who applied to the psychiatry policlinics of Ondokuz Mayıs University Medicine Faculty between September-October 2007. The inclusion criteria for the study was to have a panic attack in the last 1 month, to be in treatment (to use selective *serotonin* reuptake inhibitors), to volunteer to participate in the study, to be at least primary school graduate, and to be 18-65 years old. The patients who suffered from major depression with psychotic features, disorders related to substance use,

psychotic or bipolar disorder, organic mental disorder, dementia, general medical condition, chronic disorders that damage respiratory/circulatory and cardiac system, and the pregnant patients were excluded from the study.

Information Form: The characteristics such as age, gender, marital status, education level, economical level, age at onset, age at the patient applied for treatment, duration of treatment, drugs used, and physical illnesses were determined.

Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I): SCID-I is a structured interview developed by First and colleagues (1997) for making the major DSM-IV Axis I diagnoses. The clinical version of SCID-I was used in the present study. SCID-I was translated into Turkish by Çorapçıoğlu and colleagues (1999). The adaptation, validity and reliability studies of SCID-I have been conducted.

Manual for the Structured Clinical Interview for DSM-III-R Personality Disorders (SCID-II): SCID-II is an interview developed by Spitzer (1990) for DSM-

TABLE 3. Hierarchical multiple regression of the psychological scales that predicted the respiratory-circulatory, cognitive, and autonomic subtypes.

BAI			(0.415)
Respiratory-circulatory	0.22	1.19	0.852
Cognitive	2.01	1.19	0.095
Autonomic	0.12	1.19	0.915
ASI			(0.886)
Respiratory-circulatory	0.39	1.16	0.734
Cognitive	0.75	1.16	0.520
Autonomic	0.38	1.16	0.741
PDSS			(0.183)
Respiratory-circulatory	-0.84	0.44	0.064
Cognitive	-0.10	0.44	0.815
Autonomic	0.52	0.44	0.246
PAS			(0.146)
Respiratory-circulatory	-1.78	0.83	0.034
Cognitive	-0.46	0.83	0.575
Autonomic	-0.61	0.83	0.462

III. It was revised with DSM-III-R, and used for the diagnosis of Axis II personality disorders. SCID-II is a structured form for the individual administration. The Turkish version was developed by Sorias and colleagues (1990), and the validity-reliability study has been conducted.

Panic Attack Symptom Checklist (PASC): This checklist was created by combining the symptoms included in DSM-IV-TR diagnostic criteria for panic disorder with the symptoms that were not present in DSM-IV-TR diagnostic criteria. PASC consisted of 20 symptoms, 13 of these were the symptoms defined in DSM-IV-TR diagnostic criteria for panic disorder. The symptoms that were not present in DSM-IV-TR were originated from the clinical observations of the authors as well as the previous literature on the subject (Starcevic et al., 1993; Cox et al., 1994; Fidaner et al., 1998; Pio-Abreu et al., 1998; Örsel et al., 2003). The symptoms on the list were chosen according to the last panic attack the patient has had. The severity of panic attack were interrogated by the interviewer and scored as “0” (no occurrence), “1” (mild level), “2” (medium level), “3” (severe).

Beck Anxiety Inventory (BAI): BAI was created by Beck and colleagues based on the cognitive theory. It is a self-administered inventory used for determining the anxiety level of the individual. It is consisted of 21 somatic and cognitive anxiety symptoms. Each symptom is ranked on a 4-point scale ranging from 0 (not at all) to 3 (severe). The total score ranges from 0 to 63. The validity and reliability studies of the Turkish version were conducted by Ulusoy and colleagues (1998). The cut off

point is accepted as 17.

Anxiety Sensitivity Index (ASI): ASI measures the fear created by the anxiety symptoms or their consequences. It evaluates the degrees of situations where individuals display anxiety symptoms such as serious illness, source of shame or loss of control. ASI, which is a self-administered scale, is consisted of 16 items focusing on the anxiety related sensations. Patients score each item on a scale from 0 to 4. The total score ranges from 0 to 64. The validity and reliability studies of the Turkish version were conducted by Dilbaz and Güz (2001).

Panic Disorder Severity Scale (PDSS): PDSS is a semi-structures scale consisted of 7 items. The scale, which is scored by the professional, has high psychometric characteristics. It aims to evaluate the frequency of panic attacks, anticipatory anxiety, avoidance of physical sensations, deterioration of work related and social performance (Shear et al., 1997). Each symptom is ranked on a 4-point scale by the interviewer. The total score ranges from 0-28. The validity, reliability, and standardization studies of the Turkish form have been conducted (Monkul et al., 2004).

Panic and Agoraphobia Scale (PAS): PAS is a scale created by Bandelow (1998) for assessing the severity of panic disorder with or without agoraphobia. It takes into account the panic attacks, phobic avoidance, anticipatory anxiety, loss of ability, and preoccupations about health. There are separate forms for the clinical observation and self-report. It has 5 subscales and each question is ranked from 0 to 4. 13 items of the total 14 items are scored.

Statistical analysis: 20 symptoms presented on the Panic Attack Symptom Checklist were used for the factor-analytic study. The factors with an Eigen value over 1 were obtained at the end of the principal component analysis and varimax rotation in the factor analysis. In order to examine the predictive characteristics of these factors, the *hierarchical multiple regression* analysis was conducted with the subtitles of PAS.

RESULTS

The sample consisted of 46 male (43.8%) and 59 female (56.2%) participants. The mean age was 35.81 ± 10.78 , the mean of education duration was 10.64 ± 3.75 years, the mean age at onset was 28.97 ± 9.47 , and the mean of duration of illness was 39.35 ± 84.60 months. Among the participants, 71 (67.6%) patients had panic disorder with agoraphobia.

TABLE 4. Hierarchical multiple regression of the respiratory-circulatory, cognitive, and autonomic subtypes, with the PAS clinical variables.

	B	SS	P
Severity of panic attack			
Respiratory-circulatory	0.23	0.07	0.002**
Cognitive	0.02	0.07	0.708
Autonomic	0.02	0.07	0.721
Frequency of panic attack			
Respiratory-circulatory	0.28	0.92	0.003*
Cognitive	-0.02	0.92	0.816
Autonomic	0.02	0.92	0.756
Agoraphobia and avoidance			
Respiratory-circulatory	0.48	0.14	0.001***
Cognitive	0.17	0.14	0.222
Autonomic	-0.18	0.14	0.205
Anticipatory anxiety			
Respiratory-circulatory	-1.47	0.80	0.071
Cognitive	0.31	0.80	0.000***
Autonomic	-0.01	0.80	0.886
Loss of ability			
Respiratory-circulatory	-0.15	0.72	0.127
Cognitive	0.04	0.72	0.68
Autonomic	0.04	0.72	0.62
Having preoccupations about health			
Respiratory-circulatory			
Cognitive	0.22	0.80	0.006**
Autonomic	-0.19	0.80	0.018*
	0.16	0.80	0.048*

*P < 0.05, **P < 0.01, ***P < 0.001

A comorbid disorder was determined in 39% of the patients. The most frequently observed comorbid disorder was generalized anxiety disorder, specific phobia, major depressive disorder, and social phobia.

The mean scores of the study group were as follows: 32.7±12.2 for BAI, 32.2±11.7 for ASI, 30.5±8.6 for PAS, and 13.2±4.6 for PDSS.

The minimum number of symptoms was 9, whereas the maximum number of symptoms was 20 according to the Panic Attack Symptom Checklist (PASC). The mean for PASC was determined to be 14.57±2.48. Table 1 presents the frequency of symptoms that take place on the Panic Attack Symptom Checklist, and the mean of severity of each symptom that is scored 0 to 3.

The factor analysis was conducted using 20 symptoms on the Panic Attack Symptom Checklist. Three factors that had an Eigen value over and explained 61.75% of the total variance were obtained in the principal component analysis and varimax rotation. The three factors explained respectively 34.31%, 16.55%, and 10.88% of the total variance. These factors were named according to the predominant findings during the panic attacks.

The symptoms such as palpitation, shortness of breath, feeling of choking, chest pain/discomfort, fear of death, paresthesia, blurred vision, dryness of mouth, feeling of strangulation in the throat belonged to the first factor called as “respiratory-circulatory”. The symptoms of depersonalization/derealization, fear of going mad or losing control, discomfort, difficulty to focus, blurry mind, desperation/hopelessness belonged to the second factor named as “cognitive.” Finally, the symptoms such as perspiration, shivering/shaking, nausea/abdominal pain, dizziness/drowsiness, feeling cold/hot belonged to the third factor called as “autonomic” (Table 2).

A statistically significant relationship was not obtained from the multiple regression analysis conducted with the psychological instruments and the factor structures (Table 3). The panic attack characteristics (severity, frequency), the degree of agoraphobia, the anticipatory anxiety, the loss of ability, the belief in an organic illness that appeared on the subscales of PAS were scored between 0-4 by the patients. Then, the hierarchical multiple regression analysis was conducted using the items mentioned above and the factor structures. The panic attack severity, panic attack frequency and degree of agoraphobia were found to be strong predictors for the “respiratory-circulatory” subtype. The anticipatory anxiety was found to be a strong predictor for the cognitive subtype. The preoccupation about health was determined as a stronger predictor for respiratory-circulatory subtype, predictor for “autonomic” subtype, and a reverse predictor for the cognitive subtype. The results obtained from the hierarchical multiple regression analysis conducted with the loss of ability and the factor structures were not statistically significant (p>0.05) (Table 4).

DISCUSSION

The majority of the studies that examined the subtypes were based on the panic attack criteria defined in DSM-IV TR. On the other hand, this study examined the possible subtypes of the panic disorder by focusing on the other symptoms that could possibly appear in the course of a panic attack, in addition to the symptoms used for the diagnosis.

Most of the studies that investigated this subject used only the symptoms that were defined as the diagnostic criteria in DSM (Briggs et al. 1994; Pio-Abreu et al., 1998; Marquez et al., 2001; Meuret et al., 2006). In this case, it might not be possible to find all the symptoms cluster of the subtypes. An important point that differentiated this study from the relevant studies was that the

present study didn't only include the panic attack symptoms defined as the diagnostic criteria in DSM-IV TR, but it covered the other symptoms frequently reported by the patients. The present study showed that the panic attack symptoms that were not defined in DSM existed and they might be effective in forming the subtypes (Fidaner et al., 1998; Starcevic et al., 1993; Örsel et al., 2003; Pio-Abreu et al., 1998).

The patients who suffer from the panic disorder are prone to have chronic hyperventilation problem and the acute hyperventilation triggered by the stress may cause panic attacks. The hyperventilation may end up in respiratory alkalosis, and vasoconstriction may occur. The symptoms that appear depending on the decreased level of O₂ in the body parts are as follows: dizziness, drowsiness, shortness of breath, blurry vision, increase in the heart beat, parenthesis and prickles in arms and legs, feeling of coldness in hands and feet, and sometimes contractions in arms and legs. In the course of hyperventilation, the individual

mostly prefers breathing through chest instead of diaphragm, thus a chest pain appears after a while (Kleine, 1993; Monkul et al., 2006; Grillion, 2007). These theories make clear the reason why the symptoms of the respiratory-circulatory subtype occur. The dryness of mouth might be a possible consequence of hyperventilation. Likewise, the mucous membrane in the respiratory tract might become dry because of hyperventilation, and cause feeling of strangulation. Similar to the present study, there exist other studies, which determined that dryness of mouth and shortness of breath were in the same symptom cluster (Pio-Abreu et al., 1998; Örsel et al., 2003).

The symptom cluster of the cognitive subtype is related to some autonomic stimulations or respiratory dysregulation, but a strong fear and anxiety accompany them (Ley, 1992). There is limited biological evidence to support the cognitive subtype (Forsyth et al., 2000; Schmidt et al., 2002). Similar to the present study, most of the studies that supported the presence of the cognitive subtype clustered derealization/depersonalization and fear of going mad/loosing control symptoms together. In the present study, discomfort, difficulty to focus, blurry mind, and feelings of desperation/hopelessness symptoms were grouped under the cognitive subtype. There are other studies that reported similar findings supporting this symptom cluster (Örsel et al., 2003; Ley, 1992; Meuret et al., 2006; Cox et al., 1994).

A decrease in vagal processes is observed in patients

with panic disorder (Grillion, 2007). The symptoms such as perspiration, shivering/shaking, nausea, and feeling cold/hot were clustered in the factor called as "autonomic." There are also other studies, which came up with a similar symptom cluster (Kenardy et al., 1992; Cox et al., 1994; Örsel et al., 2003; Meuret et al., 2006).

Some studies claimed that there existed a factor named as "vestibular" (Örsel et al., 2003; Kenardy et al., 1992). The symptom cluster of the vestibular factor in those studies is similar to the autonomic subtype mentioned in the present study except the auditory symptoms.

Meuret and colleagues (2006) conducted factor analytic studies with 343 patients who had panic syndrome. The findings revealed that palpitation, shortness of breath, feeling of choking, chest pain, fear of death, and paresthesia symptoms belonged to the "cardio-respiratory" factor; perspiration, shivering, nausea, feeling cold/hot, and dizziness were belonged to the "autonomic/somatic" factor; derealization, fear of going mad and loosing control belonged to the "cognitive" factor. The mentioned study put forward a model consisted of three factors. The respiratory-circulatory factor obtained in the present study is similar to the cardio-respiratory factor obtained by Meuret and colleagues, the cognitive factor defined in this study is similar to their cognitive factor, and the autonomic factor mentioned in the present study is similar to their autonomic/somatic factor in terms of the symptom clusters. The use of the factors that are not defined in DSM-IV-TR was considered as the limitation of this study. The factor explained with the biggest variance (34.31%) in the present study was the respiratory-circulatory subtype similar to the Meuret and colleagues' study

Cox and colleagues (1994) conducted factor analytic studies and named the factor, which included the dizziness, derealization, paresthesia, feeling cold/hot, perspiration, shivering blackout, nausea, difference in vision and hearing as "dizziness". They called the factor, which included the symptoms such as shortness of breath, palpitation, chest pain, feeling of choking, and fear of death as "cardio-respiratory." Finally, they named the factor, which included the symptoms of derealization, fear of going mad/loosing control, difficulty in focusing, desire to escape, and desperation/hopelessness as "cognitive." The cardio-respiratory factor in Cox and colleagues' study is similar to the respiratory-circulatory factor in the present study, the cognitive factor is similar to the factor that is named the same, and the dizziness factor is

similar to the autonomic factor of the present study. The total variance explained in Cox and colleagues' study was 46.7%, and the factor loadings for the dizziness, cardio-respiratory, and cognitive subtypes were respectively: 28.2%, 9.9%, and 8.7%.

The factor loadings of the present study were quite different from Cox and colleagues' study in terms of the sequence. This difference may have arisen from the selection of patients. Moreover, the theories about respiratory-circulatory system, which argue that dyspnea is a core symptom, hyperventilation is often observed, there is a high CO₂ sensitivity, the subjective feeling of choking is high become predominant in the etiopathogenesis of the panic disorder (Kleine, 1993). All of the information mentioned above support the dominance of the respiratory-circulatory subtype described in the present study.

Shiori and colleagues (1996) categorized the PD symptoms into three subtypes using the cluster analysis. The first cluster consisted of symptoms such as shortness of breath, feeling of choking, perspiration, nausea, and feeling cold/hot; the second cluster included dizziness, palpitation, shivering, depersonalization, anticipatory anxiety, and agoraphobia symptoms; and the third clustered consisted of symptoms such as fear of death and going mad, paresthesia, and chest pain. The respiratory-circulatory subtype in the present study corresponded to the first and third cluster of Shiori and colleagues' study; and another factor in which the fear of going mad is dominant corresponded to the cognitive subtype of the present study. The difference in the distribution of the symptoms determined in this study conducted in Japan might be related to the cultural factors. In addition to that, the rate of patients having PD with agoraphobia (40.9%) was quite low compared to the findings in the present study. In a study conducted in Turkey defined the "cardiovascular" factor, the "cognitive" factor, the "gastrointestinal and vestibular" factor, and the "tension" factor which included paresthesia, feeling hot, muscle pain, muscle tension, and hearing difficulty (Örsel et al., 2003). The fact that 40% of the patients who participated in the study had a medical illness (1/4 of them having a cardiovascular illness) might have caused the variety of symptoms in cardiovascular and tension factors. The respiratory-circulatory and autonomic factor in the present study corresponded to the cardiovascular factor in the mentioned study.

The respiratory-circulatory subtype mentioned in the present study is similar to the respiratory subtype which is defined with the presence of at least 4 symp-

toms of shortness of breath, feeling of choking, fear of death, chest pain, and paresthesia described previously by Briggs and colleagues (1993).

Similar to the present study, other studies also categorized the derealization/depersonalization and fear of going mad/loosing control symptoms under the cognitive subtype.

Similarly, many studies included the subtype defined in the present study as autonomic. In these studies, perspiration, shivering, and dizziness were the common symptoms that belonged to this subtype (Cox et al., 1994; Meuret et al., 2006; Marquez et al., 2001; Fidaner et al., 1998; Örsel et al., 2003). Feeling cold/hot took place in the autonomic subtype in some of studies, whereas the same symptom belonged to the respiratory-circulatory subtype in the present study (Örsel et al., 2003; Kenardy et al., 1992).

The symptoms such as shortness of breath, feeling of choking, chest pain, paresthesia and fear of death clustered in the respiratory subtype by Briggs were also related to the cardiovascular system, and partially related to the central nervous system (sympathetic activation). Therefore, the "respiratory-circulatory" name that referred to two systems was preferred for the first factor. The similar naming preference has been observed in some other studies as well (Cox et al., 1994; Pio-Abreu et al., 1998; Masansa et al., 2001; Meuret et al., 2006).

There are studies which pointed to the presence of a factor consisted of gastrointestinal symptoms (Pio-Abreu et al., 1998; Starcevic et al., 1993). In the present study, nausea or abdominal pain, which is a gastrointestinal symptom, was clustered together with perspiration, shivering, dizziness, and feeling cold/hot in the autonomic factor.

67.6% of patients who attended in the study were diagnosed with PD with agoraphobia, and this rate is compatible with the literature findings (Alkın, 2000; Onur et al., 2006b; Eaton et al., 1994). Some studies showed that agoraphobia was more severe in the respiratory subtype (Briggs et al., 1993; Biber et al. 1999; Nardi et al., 2004). It was also reported that phobic avoidance was more frequently observed, agoraphobia and anticipatory anxiety was higher in the cognitive subtype (Merikangas et al., 1996). In the present study, it was revealed that agoraphobia was a predictor for the respiratory-circulatory factor.

A statistically significant relationship was not found at the end of the hierarchical multiple regression analysis

conducted with the PDSS sub-parameters and the factor structures. This might be the case because the scale was answered by the interviewer. According to the self-report forms of the PAS, severity and frequency of the panic attack, and degree of agoraphobia were found to be strong predictors for the first factor named as the respiratory-circulatory factor. Anticipatory anxiety was determined as a strong predictor for the second factor names as the cognitive subtype. Having preoccupations about health was a stronger predictor for the respiratory-circulatory subtype, a predictor for the autonomic type, and a reverse predictor for the cognitive type. The relationship between the loss of ability and the factor structures were not found to be statistically significant. In a similar factor analytical study conducted by Meuret and colleagues (2006), at the end of the multiple hierarchical regression analysis, the frequency and severity of panic attack, and the degree of agoraphobia were found to be predictors for the cardiovascular subtype, whereas the degree of anticipatory anxiety was found to be a predictor for the cognitive subtype. Moreover, the loss of ability was determined as a strong predictor for the autonomic/somatic and the cognitive subtype. In this study, approximately 60% of patients were getting medication treatment for PD, and comorbid illnesses such as asthma were observed. All the patients who attended to the present study were getting medication treatment, but they didn't have any medical

comorbid illnesses. The loss of ability in patients with PD might appear because the disorder is not treated and because of the presence of comorbid disorders. In the literature, there was not any study, which examined the relationship between having preoccupations about health and subtypes.

One of the important limitations of the present study was that the study sample only consisted of patients who applied to psychiatry polyclinics of the university. Moreover, the patients reported during the interview that the variety and severity of the symptoms that appeared in the course of panic attacks differed over the years. Therefore, it is not known what difference providing homogeneity in terms of the age at onset make in determining the subtypes. For this reason, it should be taken into account that the symptoms of the patients that had their first panic attack, that have been treated for a long time, or that applied for treatment very late might show variation. The presence of a comorbid disorder is another important factor that might affect the symptom clusters. The symptoms were evaluated independently from the individuals, because the present study was a factor analytical study. Consequently, the personal variables such as the distribution of gender and comorbid disorder could not be related to the defined subtypes. There is a need for extensive research, which will focus on this subject.

REFERENCES

- Abrams K, Rassovsky Y, Kushner MG (2006) Evidence for respiratory and nonrespiratory subtypes in panic disorder. *Depress Anxiety* 23: 474–481.
- Alkın T (2000) Panik bozukluğu ve agorafobi. Tükel R (ed.) “Anksiyete Bozuklukları”ndan. Ankara, Çizgi Tıp Yayınevi, s.5-37.
- Bandelow B, Brunner E, Broocks A et al. (1998) The use of the Panic and Agoraphobia Scale (PAS) in a Clinical Trial. *Psychiatry Res*, 16: 43-49.
- Biber B, Alkın T (1999) Panic disorder subtypes: Differential responses to CO2 challenge. *Am J Psychiatry* 156: 739–44.
- Bouwer C, Stein DJ (1997) Association of panic disorder with a history of traumatic suffocation. *Am J Psychiatry* 154: 1566–1570.
- Briggs AC, Stretch DD, Brandon S (1993) Subtyping of panic disorder by symptom profile. *Br J Psychiatry* 163: 201-209.
- Bringager CB, Gauer K, Arnesen H et al. (2008) Nonfearful panic disorder in chest-pain patients: status after nine-year follow-up. *Psychosomatics* 49: 426–437.
- Cassano GB, Petracca A, Perugi G et al. (1989) Derealization and panic attacks: a clinical evaluation 150 patients with panic disorder/agoraphobia. *Compr Psychiatry* 30: 5-12.
- Cox BJ, Swinson RP, Endler NS et al. (1994) The symptom structure of panic attacks. *Compr Psychiatry* 35: 349-353.
- Çorapcıoğlu A, Aydemir Ö, Yıldız M et al. (1999) Structured Clinical Interview for DSM-IV (SCID-I), Türkçe Formu. Ankara; Hekimler Yayın Birliği.
- Eaton WW, Kessler RC, Wittchen HU et al. (1994) Panic and panic disorder in the United States. *Am J Psychiatry* 151: 413-20.
- Dilbaz N, Güz H. Anxiety Sensitivity Index: Reliability and validity. Poster presentation [Turkish] at the 37th Turkish National Psychiatry Congress, İstanbul, 2001.
- Fidaner H, Tunca Z, Cimilli C (1998) Panik bozukluğunda atakların klinik özellikleri: Q yöntemi ile bir çalışma. *Türk Psikiyatri Dergisi* 9: 277-283.
- First MB, Spitzer LR, Gibbon M et al. (1997) Structured Clinical Interview for Axis I Disorders (SCID-I), Clinical version first publication in the United States by American Psychiatric Press Inc. Washington D.C and London, England.
- Fleet RP, Martel JP, Lavoie KL et al. (2000) Nonfearful panic disorder a variant of panic in medical patients? *Psychosomatics* 41: 311-320.
- Forsyth JP, Eifert GH, Canna MA (2000) Evoking analogue subtypes of panic attacks in a nonclinical population using carbon dioxide-enriched air. *Behav Res Ther* 38: 559-572.
- Freire RC, Lopes FL, Valença MA et al. (2008) Panic disorder respiratory subtype: A comparison between responses to hyperventilation and CO2 challenge tests. *Psychiatry Research* 157: 307–310
- Freire RC, Valença AM, Nascimento I et al. (2007) Clinical features of respiratory and nocturnal panic disorder subtypes. *Psychiatry Res* 30: 287-291.
- Goodwin RD, Hamilton SP, Milne BJ et al. (2002) Generalizability and correlates of clinically derived panic subtypes in the population. *Depress Anxiety* 15: 69-74.

- Grillion C. (2007) Anksiyete bozuklukları: Psikofizyolojik yönleri. Aydın H, Bozkurt A (çeviri ed.) "Kaplan&Sadock's Comprehensive Textbook of Psychiatry"den, sekizinci baskı, Ankara, Güneş Kitabevi, s.1728-1739.
- Hegel MT, Ferguson RJ (1997) Psychophysiological assessment of respiratory function in panic disorder: evidence for a hyperventilation subtype. *Psychosom Med* 59: 224-30.
- Horwath HE, Adams P, Wickramaratne P et al. (1997) Panic Disorder with smothering symptoms: Evidence for increased risk in first-degree relatives. *Depress Anxiety* 6: 147-153.
- Kenardy J, Evans L, Oei TPS (1992) The latent structure of anxiety symptoms in anxiety disorder. *Am J Psychiatry* 149: 1058-1061.
- Kircanski K, Craske MG, Epstein AM et al. (2008) Subtypes of panic attacks: a critical review of the empirical literature. *Depression and Anxiety* 0:1-10.
- Kleine DF (1993) False suffocation alarms, spontaneous panics, and related conditions: an integrative hypothesis. *Arch Gen Psychiatry* 50: 306-317.
- Lelliot P, Bass C (1990) Symptom specificity in patients with panic. *Br J Psychiatry* 157: 593-597.
- Ley (1992) The many faces of PAN. Psychological and physiological differences among three types of panic attacks. *Behav Res Ther* 30: 347-57.
- Marquez M, Segui J, Garcia L et al. (2001) Is panic disorder with psychosensorial symptoms (Depersonalization-Derealization) a more severe clinical subtype? *J Nerv Ment Dis* 189: 332-335.
- Massana J, Lopez Risueno JA, Massana G et al. (2001) Subtyping of panic disorder patients with bradycardia. *Eur Psychiatry* 16: 109-114.
- Merikangas KR, Angst J, Eaton W et al. (1996) Comorbidity and boundaries of affective disorders with anxiety disorders and substance misuse: Results of an international task force. *Br J Psychiatry* 168: 58-67.
- Meuret AE, White KS, Ritz T et al. (2006) Panic attack symptom dimensions and their relationship to illness characteristics in panic disorder. *J Psychiatr Res* 40: 520-527.
- Monkul ES, Tural U, Onur E et al. (2004) Panic disorder severity scale: Reliability and validity of the Turkish version. *Depress Anxiety* 20: 8-16.
- Monkul S, Alkın T, Onur E (2006) Panik bozukluğun patogenezi. Tükel R, Alkın T (ed.) "Anksiyete bozuklukları"ndan, 1. Baskı, Ankara, Pozitif Matbaacılık, s.69-98.
- Moynihan JE, Gevirtz RN (2001). Respiratory and cognitive subtypes of panic. *Behav Modif* 25: 555-583.
- Nardi AE, Valenca AM, Lopez FL et al. (2006) Psychopathological profile of 35% CO2 challenge test-induced panic attacks: a comparison with spontaneous panic attacks. *Compr Psychiatry* 47:209-214.
- Nardi AE, Valenca AM, Nascimento I et al. (2004) Psychopathological description of hyperventilation-induced panic attacks: A comparison with spontaneous panic attacks. *Psychopathology* 37:29-35.
- Onur E, Alkın T, Tural Ü (2006a) Panic disorder subtypes: Further clinical differences. *Depress and Anxiety* 0:1-8.
- Onur E, Monkul S, Alkın T (2006b) Panik bozukluğunun fenomenolojisi. Tükel R, Alkın T (ed.) "Anksiyete bozuklukları"ndan, 1. Baskı, Ankara, pozitif matbaacılık, s.41-67.
- Örsel S, Güriz O, Akdemir A et al. (2003) Panik bozukluğu alt tiplerinin belirtiler açısından araştırılması *Klinik Psikiyatri* 6: 204-212.
- Pio-Abreu JL, Ramalheira C, Valenta JM (1998) Towards a "map" of panic: structure of the bodily symptoms. *Acta Psychiatr Scand* 97: 66-70.
- Russell JL, Kushner MG, Beitman BD et al. (1991) Nonfearful panic disorder in neurology patients validated by lactate challenge. *Am J Psychiatry* 148: 361-364.
- Sansoy G, Böke Ö, Arık AC et al. (2008) Panic disorder with nocturnal panic attacks: symptoms and comorbidities. *Eur Psychiatry* 23: 195-200.
- Schmidt NB, Forsyth JP, Santiago HT et al. (2002) Classification of panic attack subtypes in patient and normal controls in response to biological challenge: implications for assessment and treatment. *J Anxiety Disord* 16: 625-638.
- Segui J, Marquez M, Garcia L et al. (2000a) Depersonalization in panic disorder: A clinical study. *Compr Psychiatry* 41: 172-178.
- Segui J, Marquez M, Canet J et al. (2000b) Differential clinical features of late-onset panic disorder. *J Affect Disord* 57: 115-119.
- Segui J, Marquez M, Garsia L et al. (1999) Differential clinical features of early-onset panic disorder. *J Affect Disord* 54: 109-117.
- Shear MK, Brown TA, Barlow DH et al. (1997) Multi-center, collaborative Panic Disorder Severity Scale. *Am J Psychiatry* 54: 571-575.
- Sheikh JI, Leskin GA, Klein DF (2002) Gender differences in panic disorder: findings from the national comorbidity survey. *Am J Psychiatry* 159: 55-58.
- Shiori T, Someya T, Murashita J et al. (1996) The symptom structure of panic disorder: a trial using factor and cluster analysis. *Acta Psychiatr Scand* 93: 80-86.
- Sorias S, Saygılı R, Elbi H et al. (1990) DSM-III-R yapılandırılmış klinik görüşmesi-Kişilik bozuklukları formu. Ege Üniversitesi Basımevi, İzmir.
- Spitzer RL, Williams JBW, Gibbon M et al. (1990) Structured clinical interview for DSM-III-R personality disorders (SCID-II). New York, New York State Psychiatric Institute, Biometrics Research.
- Starcevic V, Kellner R, Uhlenhuth EH et al. (1993) The phenomenology of panic attacks in panic disorder with and without agoraphobia. *Compr Psychiatry* 34:36-41.
- Telch MJ, Jacquin K, Smits JA et al. (2003) Emotional responding to hyperventilation as a predictor of agoraphobia status among individuals suffering from panic disorder. *J Behav Ther Exp Psychiatry* 34:161-70.
- Ulusoy M, Şahin N, Erkmen H. (1998) Turkish Version of the Beck Anxiety Inventory. *J Cogn Psychoter* 12:163-172.
- Valenca AM, Nardi AE, Nascimento I et al. (2002) Respiratory panic disorder subtype and sensitivity to the carbon dioxide challenge test. *Braz J Med Biol Res* 35:783-788.
- Verburg K, Griez E, Meijer J et al., (1995) Respiratory disorders as a possible predisposing factor for panic disorder. *J Affect Disord* 33: 129-134.