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Semiology and subtyping of panic disorders

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To date, the quantitative psychopathology of panic disorder (PD) has been less well studied than that of other psychiatric conditions such as schizophrenia or major depression. The aim of the present study was to assess the frequency and factorial grouping of symptoms in a naturalistic sample of PD patients. A total of 274 consecutive cases of PD who contacted an out-patient clinic in Barcelona, Spain were assessed by two experienced interviewers. The assessment instruments included the Structured Clinical Interview for DSM-III-R Upjohn version (SCID-UP-R) and an inventory of panic attack symptoms based on DSM-III-R. Of the patients who presented at the unit during the assessment period, 8.5% presented with PD. Palpitations, shortness of breath, fear of dying and dizziness were the most frequent and intense symptoms reported by the PD patients. Principal-component analysis revealed four factors which accounted for 57% of the variance, including 'cardiorespiratory' (26.1%) and 'vestibular' (15.1%) factors, and two additional factors with mixed symptoms. The frequency of presentation of symptoms was similar to that reported in other studies. However, some discrepancies were observed that may be attributed to transcultural differences as well as to terminological problems and the range of symptoms assessed. These factors may also explain some of the differences found in factor analysis groupings in previous studies. Our findings support the symptom subtyping of PD.

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Key words: panic attack; panic disorder; psychopathology

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Introduction

Panic disorder (PD) is a frequently encountered psychiatric condition. The lifetime prevalence of PD has been estimated to be 3.5–3.8% in recent studies (1). With regard to its natural history, panic disorder tends to appear in young people, reaching its highest prevalence between 25 and 44 years of age. Its frequency is twice as high in women as in men. Some authors have referred to a bimodal distribution, with a first peak for both sexes between 15 and 24 years of age, and a second peak between 45 and 54 years (1). Other studies have analysed aspects related to the course of the disorder, both in the general population (2) and in clinical settings, such as the Harvard/Brown Anxiety Research Project (HARP) (3).

One aspect which has aroused increasing interest during the last decade concerns the semiology of PD (4–6). Different authors have suggested that PD is not a homogeneous disorder, and that there are differences between those disorders with or without agoraphobia (7–9), or differences in their predominant symptoms (5, 10–17). Starcevic et al. (8) have divided symptoms into 'first rank' and 'second rank', with the first rank including the more frequent and severe symptoms, such as palpitations, tachycardia, dyspnoea, feelings of instability or dizziness, and trembling. Less frequent and generally less serious are the 'second-rank' symptoms, such as choking, chest pain, paraesthesias, hot flushes, depersonalization/derealization and nausea. Several authors have pointed out the lack of a sufficient number of semiological empirical studies which validate the standardized criteria in use (5, 13). Other authors have suggested a possible typification of PD based on predominant symptoms. Thus some investigators have differentiated between PD with cardiorespiratory symptoms (13), PD with vestibular symptoms (11), PD with gastrointestinal symptoms (12, 13), and PD with depersonalization/derealization (10), or without a subjective feeling of fear (18).

These clinical data are complemented by information derived from exploratory factor studies of anxious disorders (9, 19–25), in which cardiorespiratory and vestibular factors tend to explain the largest percentage of variance. It is important to bear in mind that just five out of eight studies

specifically refer to panic disorder patients (9, 22–25). Other factor groupings that appear in the literature are cognitive symptoms, depersonalization, paraesthesias and autonomic activation. This clinical heterogeneity can have important implications so far as aetiology, course and treatment are concerned (15). On the other hand, there are transcultural differences which can influence the clinical presentation of the disorder. Thus Liebowitz et al. (26) pointed out how 'ataques de nervios' (literally, 'nerve attacks') in a Hispanic population in New York were associated with panic symptoms, even when the patients failed to meet the criteria for this disorder. Other studies have explored the symptom differences between northern and southern countries (27). The aim of the present study is to contribute to the clinical subtypification of PD in our cultural environment, by analysing a sample of consecutive PD cases evaluated at their first clinical consultation at two centres in the same urban area, by the same health care team.

Material and methods

Subjects

The study sample consisted of a series of 274 patients over 16 years old, of both sexes, suffering from PD, who were consecutively assessed at the Section of Psychiatry, La Alianza General Hospital. This centre is part of the area's most important health management organization (HMO). The study lasted for 4 years, starting at the time when this unit was first established (1 March 1991–28 February 1995). Of the 3206 patients who were examined at the unit during the assessment period, 8.5% (n=274) presented with PD. Of this sample, 76.4% were women. The mean age at the time of the interview was 44.1 years (range 16–77 years). Single people represented 20.8% of the group, while 69.0% were married, 3.3% were separated or divorced and 6.9% were widowed. The mean age at onset of PD was 35.9 years (range 10–76 years), and the mean duration of PD was 8.2 years (range 0.1–57.9 years).

Subjects were excluded from the study if PD was clearly secondary to some other medical pathology, or associated with organic brain disorders, according to DSM-III-R criteria. In patients over 60 years of age, a final diagnosis was delayed until any other possible medical causes could be ruled out. Thyroid tests were performed on all patients, as well as ECG, chest X-ray and a neurological examination. Among those patients with thyroid pathology, only subjects with normal thyroid levels whose dysfunction was compensated (according to an endocrinological report) were included.

Procedure

Clinical assessment was made by two experienced interviewers, either a psychiatrist (J.S.) or a clinical psychologist (J.C.), according to DSM-III-R criteria. The Structural Clinical Interview for DSM-III-R — Patient Version (SCID-UP-R) was used for Axis-I diagnosis (28). The presence of comorbid psychiatric pathology was also investigated, again following DSM-III-R criteria. Diagnostic groups were included in two cases, namely drug dependency (which included alcoholism and other drug dependencies, with a small number of cases in the latter group) and eating disorders (anorexia nervosa and bulimia). Diagnostic reliability was checked by two independent evaluators, using a group of 30 patients, and yielding a kappa value of 0.8 for Axis I. Patients over 60 years of age were also administered the Spanish version (29) of the Mini-Mental State Examination (30).

A 14-item inventory of panic attack symptoms, based on DSM-III-R symptoms, was used. We separated the symptoms 'faintness' and 'dizziness' into two categories rather than one as appears in the SCID-UP-R (31). This self-administered inventory uses a 4-point Likert scale, ranging from 0 to 3, to assess the severity of the symptoms (where 0=non-existent, 1=mild, 2=moderate and 3=severe).

Data analysis

The statistical tests used were Student's t-test or ANOVA for continuous variables, and the Chi-square test with Yates' correction or Fisher's exact test, when necessary, for categorical variables. The minimum level of significance was set at $P<0.05$. An exploratory factor analysis of the principal components of the 15 items on the test was performed, with varimax rotation. The number of factors was determined by applying the criterion of an eigenvalue greater than 1.

Results

Distribution of the symptoms associated with panic attacks

The most frequent symptoms reported by the 274 patients were palpitations (85.0%), shortness of breath (72.6%), fear of dying (65.7%), dizziness (62.8%), trembling (56.6%), chest pain (56.2%), faintness (53.6%), sweating (51.8%), paraesthesias or tingling sensation (48.9%) and hot flushes (46.0%). The least frequent symptoms were choking (34.7%), nausea (29.2%), depersonalization or derealization (25.5%) and fear of going crazy (24.1%). The most severe symptoms were also those most frequently cited above, namely palpitations (2.2±1.0), dyspnoea

(1.7±1.2), fear of dying (1.6±1.3) and dizziness (1.5±1.3). Chest pain also showed high severity ratings (1.3±1.3). No differences were found between the sexes with regard to the distribution or intensity of the symptoms.

The list of specific symptoms in the group of patients with agoraphobia (including in this group those patients with limited phobic avoidance) and the group of patients with uncomplicated PD was also examined. The agoraphobic patients presented more frequently with dizziness and faintness. Patients with agoraphobia reported a higher severity of dizziness, faintness, depersonalization or derealization and fear of going crazy or losing control (Table 1).

An analysis of three age groups (<40 years, 40–60 years and >60 years) showed a significant decrease in both the frequency and the intensity of symptoms as patients grew older, except for choking, chest pain, faintness, paraesthesias and fear of dying (Table 2).

Factor analysis

Principal-component analysis using a varimax rotation detected four factors which accounted for 57% of the variance (Table 3). The first factor determined 26.1% of this variance, and was related to the 'cardiorespiratory' group of symptoms. The symptoms with the highest coefficient were chest pain, palpitations, dyspnoea, paraesthesias and trembling. A cognitive symptom (fear of dying) also appeared in this factor. The second factor accounted for 15.1% of the variance and included 'vestibular' symptoms (dizziness and faintness) and cognitive symptoms such as fear of going crazy or losing control. The third factor included symptoms such as sweating, depersonalization or derealization, choking and hot flushes. This factor accounted for 8.5% of the variance. The fourth factor accounted for 7.2% of the variance and included gastrointestinal symptoms (nausea or abdominal distress) and trembling, hot flushes and paraesthesias.

Although the four components had eigenvalues greater than 1, a scree test indicated that only the first two factors were significant, while factors 3 and 4 did not contribute significantly to further explanations of variance.

Discussion

The frequency of presentation of panic symptoms was similar to that reported in other clinical studies (4, 5, 7–9, 31). Our results are in quite close agreement with those of Starcevic et al. (8), although we disagree with the terminology used by those authors. There were clear differences in the manifestation of some cognitive symptoms, compared with the US (5–9) and UK (20) studies mentioned above. In our study, fear of dying was more frequent, while fear of going crazy or losing control appeared very rarely. Fear of dying was found to be much more common in southern Europe and South America than in northern Europe and the USA in a previous cross-cultural study (27).

With regard to the intensity of the symptomatology, Cox et al. (9) have pointed out the existence of various symptoms which were not included in the DSM-IV, and which were not evaluated in our study (including thoughts of escape, feelings of helplessness, difficulty in concentrating and fear of 'causing a scene'). These symptoms, which are frequently reported by patients, indicate the need

Table 1. Frequency and intensity of patients' symptoms according to level of agoraphobia

	Frequency of symptoms				Intensity of symptoms			
	Uncomplicated ($n=64$)	Agoraphobia ($n=210$)	χ^2	P-value	Uncomplicated ($n=64$)	Agoraphobia ($n=210$)	t	P-value
Dyspnoea	43 (67.2%)	156 (74.3%)			1.58±1.22	1.77±1.22		
Choking	21 (32.8%)	74 (35.2%)			0.61±0.95	0.72±1.04		
Palpitations	54 (84.4%)	179 (85.2%)			2.25±1.08	2.20±1.09		
Chest pain	37 (57.8%)	117 (55.7%)			1.31±1.27	1.30±1.27		
Sweating	30 (46.9%)	112 (53.3%)			0.94±1.13	1.12±1.13		
Faintness	27 (42.2%)	120 (57.1%)	4.41	<0.05	0.73±1.18	0.98±1.17	−3.01	<0.01
Dizziness	32 (50.0%)	140 (66.7%)	5.83	<0.05	1.03±1.21	1.67±1.32	−3.63	<0.0001
Nausea	16 (25.0%)	64 (30.5%)			0.45±0.83	0.56±0.94		
Depersonalization	11 (17.2%)	59 (28.1%)	3.07	<0.01	0.31±0.71	0.53±0.93	−1.97	<0.05
Paraesthesias	31 (48.4%)	103 (49.0%)			0.89±1.04	1.02±1.13		
Hot flushes	31 (48.4%)	95 (45.2%)			0.80±0.95	0.84±1.03		
Trembling	35 (54.7%)	120 (57.1%)			1.12±1.11	1.19±1.13		
Fear of dying	47 (73.4%)	133 (63.3%)			1.80±1.22	1.60±1.33		
Fear of going crazy	10 (15.6%)	56 (26.7%)	3.27	<0.01	0.38±0.92	0.65±1.12	−1.97	<0.05

Table 2. Frequency and intensity of patients' symptoms according to age of onset

	Frequency of symptoms					Intensity of symptoms				
	<40 years (n=176)	40–60 years (n=72)	>60 years (n=26)	χ^2	P-value	<40 years (n=176)	40–60 years (n=72)	>60 years (n=26)	F	P-value
Dyspnoea	133 (75.6%)	53 (73.6%)	13 (50.0%)	7.49	<0.05	1.82±1.21	1.69±1.18	1.12±1.24	3.92	<0.05
Choking	68 (38.6%)	21 (29.2%)	6 (23.1%)			0.78±1.06	0.60±0.99	0.42±0.81		
Palpitations	156 (88.6%)	61 (84.7%)	16 (61.5%)	13.08	<0.01	2.36±1.02	2.11±1.07	1.50±1.30	7.99	<0.001
Chest pain	103 (58.5%)	41 (56.9%)	10 (38.5%)			1.33±1.25	1.35±1.29	1.00±1.33		
Sweating	105 (59.7%)	32 (44.4%)	5 (19.2%)	16.96	<0.001	1.23±1.12	0.93±1.13	0.42±0.90	6.90	<0.001
Faintness	101 (57.4%)	30 (41.7%)	16 (61.5%)	5.79	<0.05	1.16±1.16	0.83±1.11	1.15±1.08		
Dizziness	118 (67.0%)	36 (50.0%)	18 (69.2%)	6.86	<0.05	1.64±1.32	1.15±1.29	1.77±1.31	3.99	<0.05
Nausea	62 (35.2%)	13 (18.1%)	5 (19.2%)	8.66	<0.05	0.66±0.99	0.32±0.77	0.27±0.60	4.97	<0.01
Depersonalization	56 (31.8%)	12 (16.7%)	2 (7.7%)	10.98	<0.01	0.59±0.95	0.32±0.77	0.19±0.69	3.84	<0.05
Paraesthesias	94 (53.4%)	32 (44.4%)	8 (30.8%)			1.09±1.13	0.86±1.04	0.69±1.09		
Hot flushes	99 (56.3%)	18 (25.0%)	9 (34.6%)	21.58	<0.001	1.03±1.04	0.42±0.80	0.62±0.90	10.79	<0.001
Trembling	113 (64.2%)	33 (45.8%)	9 (34.6%)	12.65	<0.01	1.33±1.12	0.96±1.11	0.69±5.58	5.58	<0.01
Fear of dying	116 (65.9%)	51 (70.8%)	13 (50.0%)			1.70±1.33	1.68±1.23	1.19±1.33		
Fear of going crazy	52 (29.5%)	11 (15.3%)	3 (11.5%)	8.16	<0.05	0.74±1.18	0.33±0.86	0.23±0.65	5.29	<0.01

to revise the symptoms lists which are generally used in assessment of PD. The 'A' criterion of standard diagnostic manuals should include other symptoms that are not directly related to the panic attacks themselves, such as health worries, and feelings of dependence on and attachment to relatives. The approach to anticipatory anxiety and phobic avoidance in diagnostic manuals should be reconsidered as well. Some studies have pointed out the lack of specificity of panic attack symptoms (26). In fact, in the diagnosis of PD, excessive weight may be given to some panic attack symptoms compared to other symptoms of the illness. An example of a similar phenomenon was the overestimation of positive symptoms in the diagnosis of schizophrenia in previous classification manuals (32).

The absence of significant differences between the sexes with regard to the frequency and intensity of the symptoms is consistent with the findings of Cox et al. (9). The lower intensity of symptoms at more advanced ages is in agreement with the results of a study by Sheik et al. (33), and suggests the possibility of an additional subtype — PD of the aged — which is to be analysed in another publication. It has been suggested that a decrease in noradrenergic activity, related to ageing, could explain the lower intensity of PD symptoms in older patients (34). With regard to subclassification based on the presence of agoraphobia, other studies

Table 3. Analysis of principal components with varimax rotation of the 14-item inventory of panic attack symptoms

	Factor 1 (cardiorespiratory)	Factor 2 (vestibular)	Factor 3 (mixed)	Factor 4 (general arousal)
Chest pain	0.71			
Palpitations	0.68			
Dyspnoea	0.62			
Fear of dying	0.58			
Paraesthesias	0.58			0.52
Faintness		0.89		
Dizziness		0.88		
Fear of going crazy		0.43		
Sweating			0.73	
Depersonalization			0.59	0.41
Choking			0.59	
Nausea				0.69
Trembling	0.46			0.60
Hot flushes			0.46	0.49
Eigenvalue	3.66	2.12	1.19	1.01
Percentage of total variance (57%)	26.1%	15.1%	8.5%	7.2%

have found a higher frequency and intensity of different symptoms in patients with phobic avoidance (8). Those authors suggest the existence of a cause-and-effect relationship between some cognitive symptoms, such as depersonalization and fear of losing control, and the appearance of agoraphobia. Other authors have reported a relationship between dizziness and agoraphobia (25), consistent with our own results. The degree of phobic avoidance and the severity of symptoms were found to be unrelated in other studies (9).

Five previous studies in the literature applied an exploratory factor analysis of PD symptoms (9, 22–25). Some major differences are apparent in symptom distribution and factorization across studies. Although the type of factor analysis performed (principal-component analysis) was the same in all studies, some of these differences can be attributed to methodological aspects such as inadequate sample size (23), or the number of symptoms included in the analysis. Cox et al. analysed 23 symptoms, while other studies included 13 or 14 symptoms in the analysis (22, 23, 25). Despite these relevant differences, it is important to take into account the finding of a cardiorespiratory factor as either the first (24) or the second factor (9, 22). The vestibular factor has been found as the first factor in three previous studies (9, 22, 25). Differences in cultural expression and aspects related to conceptual translation should be considered when interpreting our data. For example, there are subtle semantic differences between the concept of choking in English and 'atragantamiento' in Spanish. Similarly, the terms suffocation and 'sofocación' are not equivalent, and have different connotations. The influence of this transcultural variation in the Spanish translation of DSM-III and DSM-IV has not been properly assessed. The careful process of back-translation that is usually applied to rating scales and psychiatric interviews needs to be applied here as well. These differences contribute to transcultural variation in the expression of PD symptoms (27).

The association of the cognitive symptom 'fear of dying' with the factor of cardiorespiratory symptoms is consistent with the findings of other authors (9, 24). In any case, the factor weight of this specific symptom was not very high (0.53), as in the study by Cox et al. (9), in which it was reported to be 0.41. For some authors, the cognitive symptom 'fear of dying' would be related more closely to the general factor of anxiety than to strong physical sensations (8). Fear of going crazy or losing control has been related to other symptoms, such as choking and nausea (9), or to other cognitive symptoms, such as depersonalization or derealization (22, 23) or fear of causing a scene, thoughts of escape and feelings of helplessness (9). In the present study this symptom was associated with dizziness and faintness, as was also found in the study by Briggs et al. (22).

More than 30 years after it was first categorized by Klein (35), the lack of published research on the semiology of PD, compared to other psychiatric disorders, is surprising, especially in view of the fact that some data seem to indicate that it could be a heterogeneous entity, with the coexistence of various clinical subgroups (15). The results of exploratory factor studies, such as the investigation reported here, are orientative and should be backed up by confirmatory studies, and it is evident that they require the use of inventories of symptoms that are even more wide-ranging than those employed by Cox et al. (9). The identification of subtypes should be compared with data on the course and outcome of the disorder, its biological characteristics, and its response to different kinds of treatment.

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