The Spectrum of Anxiety Disorders in the Medically Ill

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***Objective*:** The purpose of this cross-sectional study was to assess the prevalence and characteristics of anxiety disorders in the medically ill.

Method: A sample of 1,660 medical patients was recruited from different medical settings in different periods from 1996 to 2007. All patients underwent detailed semistructured interviews with the Structured Clinical Interview for *DSM-IV* (SCID) and the Structured Interview for Diagnostic Criteria for Psychosomatic Research (DCPR).

Results: Generalized anxiety disorder was the most frequent anxiety disturbance (10.3%) and was associated with DCPR somatization syndromes, Type A behavior, and irritable mood. Panic disorder with agoraphobia and agoraphobia without history of panic disorder had almost identical prevalence (about 4.5%), but differed in some patterns of somatization. Agoraphobia without panic attacks was related to illness denial, persistent somatization, anniversary reactions, and demoralization. Much lower prevalence rates were reported for social phobia and obsessive-compulsive disorder.

Conclusions: The findings indicate that anxiety disorders are common in the setting of medical disease and are associated with several types of psychosomatic presentations. The links between agoraphobia without history of panic disorder and illness denial may provide an explanation for some discrepancies that have occurred in the literature as to the prevalence of agoraphobia in clinical samples compared to epidemiologic studies.

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Anxiety disorders are strongly associated with chronic medical illness and physical disability.[1] However, their specific features in the setting of medical disease have attracted limited attention compared to the literature that is available on mood disorders.[2]

The aim of this study was to provide information on the prevalence and characteristics of anxiety disturbances using a large database encompassing a variety of medical settings. The association of anxiety with psychosomatic syndromes and clusters, as defined by the Diagnostic Criteria for Psychosomatic Research (DCPR),[2] was explored. The DCPR are a set of diagnostic criteria that were developed and validated by an international group of investigators to identify psychological constructs derived from psychosomatic research.[2] They encompass abnormal illness behavior (disease phobia, thanatophobia, health anxiety, illness denial), somatization syndromes (persistent somatization, functional somatic symptoms secondary to a psychiatric disorder, conversion symptoms, anniversary reactions), demoralization, irritable mood, Type A behavior, and alexithymia.

METHOD

Patients were recruited in different periods from 1996 to 2007 from different medical settings included in an ongoing multicenter project concerned with the psychosocial dimensions of medical patients.[2] Although studies involved in the research project had different aims and sample sizes, they shared a common methodology in the assessment of psychopathology and psychosocial syndromes. Patients were recruited consecutively, with the intent of being representative of their respective patient populations:

1. Consecutive outpatients with functional gastrointestinal disorders (n = 190, 11.4% of the current total sample) from the Functional Gastrointestinal Disorders Outpatient Clinic of the Scientific Institute of Gastroenterology (Castellana Grotte, Italy).
2. Consecutive outpatients with heart diseases (n = 351, 21.1%) from 3 different sources: (1) 198 outpatients who underwent heart transplantation from the Heart Transplantation Unit of the Institute of Cardiology at S. Orsola Hospital of Bologna, Italy; (2) 61 consecutive patients with a recent (within 1 month) first myocardial infarction diagnosis from the Cardiac Rehabilitation Program of the Bellaria Hospital in Bologna, Italy; and (3) 92 consecutive outpatients with a recent (within 1 month) first myocardial infarction diagnosis from the Institute of Cardiology of University Hospital in Modena, Italy.
3. Consecutive outpatients with endocrine disorders (n = 162, 9.8%) from the Division of Endocrinology of the University of Padova Medical Center, Padova, Italy.
4. Consecutive outpatients who had received a diagnosis of cancer within the past 18 months (n = 104, 6.3%) from the S. Anna University Hospital in Ferrara, Italy.
5. Consecutive outpatients with skin disorders (n = 545, 32.8%) from the Dermopathic Institute of the Immaculate, Rome, Italy.

6. Consecutive inpatients referred for psychiatric consultation in 2 large university-based general hospitals (n = 208, 12.5%) from the University of Perugia and University of Foggia, Italy.
7. Selected outpatients recruited from a large primary clinic (n = 100, 6.0%) from Modena, Italy, representing the most frequent and the least frequent attendees.

The study was approved by an institutional review board, and written informed consent was obtained from all patients. The patients who were approached were 1,830; 170 (9.3%) declined to participate. The most common reason for refusal was lack of time. The total sample thus included 1,660 patients (746 men, 44.9%, and 914 women, 55.1%) with a mean age of 45 (SD = 15.02) years and a mean of 10.5 (SD = 3.98) years of education. There were no significant differences in terms of sociodemographic variables between the patients who accepted and those who refused.

All patients underwent 2 detailed semistructured interviews by clinical psychologists or psychiatrists with extensive experience in psychiatry, clinical psychology, and psychosomatic research. Anxiety disorders (panic disorder with and without agoraphobia, agoraphobia without history of panic disorder, specific phobias, social phobia, obsessive-compulsive disorder, generalized anxiety disorder, anxiety disorder not otherwise specified) were investigated with the Structured Clinical Interview for *DSM-IV* (SCID).[3] The diagnosis of posttraumatic stress disorder was not included in the interview. Psychosomatic syndromes were diagnosed with the Structured Interview for DCPR.[2] The interview for DCPR consists of 58 items scored in a yes-or-no response format evaluating the presence of 1 or more of 12 psychosomatic syndromes (alexithymia, Type A behavior, irritable mood, demoralization, disease phobia, thanatophobia, health anxiety, illness denial, functional somatic symptoms secondary to a psychiatric disorder, persistent somatization, conversion symptoms, and anniversary reaction). The interview has shown excellent interrater reliability, construct validity, and predictive validity for psychosocial functioning and treatment outcome.[4] The χ^2 test was used to assess differences in DCPR syndromes across groups.

RESULTS

Patients diagnosed with at least 1 anxiety disorder were 390 (23.5%); 117 (30.0%) had comorbidities with other Axis I disorders. Table 1 shows the frequency of each anxiety disorder in the different medical settings according to *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (*DSM-IV*) criteria.

Generalized anxiety disorder (GAD) was the most frequent anxiety diagnosis (10.3%). Panic disorder with agoraphobia and agoraphobia without history of panic disorder had almost identical prevalence (4.6% and 4.5%, respectively). Less frequent were specific phobias (1.8%), panic disorder without agoraphobia (1.5%), obsessive-compulsive disorder (1.6%), social phobia (0.7%), and anxiety disorder not otherwise specified (0.2%). For assessing the psychosomatic correlates of anxiety disturbances, the prevalence of DCPR diagnoses in each anxiety disorder was determined (Table 2).

Patients with panic disorder with agoraphobia and agoraphobia without panic attacks shared some clinically relevant characteristics of abnormal illness behavior (significant associations with the DCPR syndromes of health anxiety and disease phobia), patterns of somatization (significant associations with functional somatic symptoms secondary to a psychiatric disorder), and irritability. However, patients with agoraphobia without panic showed further unique, distinct associations with demoralization, persistent somatization, anniversary reaction, and, particularly, illness denial.

Patients with generalized anxiety disorder had higher prevalence of health anxiety, functional somatic symptoms secondary to a psychiatric disorder, persistent somatization, anniversary reaction, Type A behavior, and irritable mood. Obsessive-compulsive disorder was significantly related to disease phobia, thanatophobia, Type A behavior, irritable mood, and demoralization.

Social phobia did not display any significant associations with DCPR syndromes, whereas specific phobias had higher prevalence of demoralization.

DISCUSSION

The findings of this study have considerable limitations. First, the population sample was heterogeneous, since it consisted of patients recruited from very different settings (inpatient versus outpatient facilities; tertiary care versus primary care versus consultation activities). Second, in many cases, patients were recruited from consecutive and unselected series; in other cases, they reflected a request from consultation or specific investigation purposes (eg, frequent attenders). Finally, establishing psychiatric diagnoses in the setting of medical disease is a difficult task, which many times is hindered by medical comorbidity and drugs.[5,6] Nonetheless, this investigation has yielded important clinical implications, and the heterogeneity of the population sample could also be one of the strengths of the study, in the sense that the spectrum of anxiety disturbances was explored in the most diverse clinical situations.

In terms of diagnostic distribution of the anxiety spectrum, the most striking finding was the roughly equivalent prevalence of *DSM-IV* panic disorder with agoraphobia (4.6%) and agoraphobia without history of panic disorder (4.5%). There is considerable controversy on the prevalence and validity of this latter diagnosis in clinical settings.[7–9] Its well-established prevalence in epidemiologic samples, as confirmed by careful recent investigations,[10–12] has been explained on the basis of a higher likelihood of lay interviewers to diagnose it compared to clinical investigators.[7] Our study, which employed experienced clinical interviewers (MD or PhD with at least 3 years of clinical experience and specific training for recognizing the subclinical manifestations of

Table 1. Prevalence of Diagnoses of Anxiety Disorders in Different Medical Settings (N = 1,660)[a]

Setting	Panic Disorder With Agoraphobia	Agoraphobia	Generalized Anxiety Disorder	Social Phobia	Obsessive-Compulsive Disorder	Specific Phobias	Any Anxiety Disorder
Within the total sample	76 (4.6)	75 (4.5)	171 (10.3)	12 (0.7)	26 (1.6)	30 (1.8)	390 (23.5)
Gastroenterology (n = 190)	6 (3.2)	11 (5.8)	20 (10.5)	0 (0)	0 (0)	0 (0)	37 (19.5)
Cardiology (n = 351)	19 (5.4)	22 (6.3)	30 (8.5)	7 (2.0)	16 (4.6)	14 (4.0)	108 (30.8)
Endocrinology (n = 162)	7 (4.3)	11 (6.8)	45 (27.8)	0 (0)	0 (0)	0 (0)	63 (38.9)
Oncology (n = 104)	0 (0)	0 (0)	4 (3.8)	0 (0)	0 (0)	0 (0)	4 (3.8)
Dermatology (n = 545)	19 (6.7)	12 (2.2)	24 (4.4)	5 (0.9)	5 (0.9)	16 (2.9)	81 (14.9)
Consultation-liaison psychiatry (n = 208)	14 (6.7)	0 (0)	35 (16.8)	0 (0)	5 (2.4)	0 (0)	54 (26.0)
Primary care (n = 100)	11 (11.0)	19 (19.0)	13 (13.0)	0 (0)	0 (0)	0 (0)	43 (43.0)

[a]All data displayed as n (%).

Table 2. Prevalence of DCPR Diagnoses in Each Anxiety Disorder[a]

DCPR Diagnosis	Panic Disorder With Agoraphobia (n = 74)[b]	Agoraphobia (n = 64)[c]	Generalized Anxiety Disorder (n = 171)	Social Phobia (n = 12)	Obsessive-Compulsive Disorder (n = 26)	Specific Phobias (n = 30)
Health anxiety						
n (%)	23 (31.1)	20 (31.2)	44 (25.7)	1 (8.3)	8 (30.8)	5 (16.7)
χ^2 (*P*)	9.70 (.002)	5.05 (.025)	9.97 (.002)	0.64 (.422)	3.55 (.059)	0.01 (.961)
Disease phobia						
n (%)	20 (27.0)	11 (17.2)	18 (10.5)	0 (0)	5 (19.2)	3 (10.0)
χ^2 (*P*)	46.43 (.000)	7.30 (.007)	3.83 (.050)	0.81 (.368)	7.53 (.006)	0.72 (.397)
Illness denial						
n (%)	9 (12.2)	16 (25.0)	13 (7.6)	1 (8.3)	2 (7.7)	2 (6.7)
χ^2 (*P*)	1.01 (.317)	15.85 (.000)	0.28 (.595)	0.42 (.519)	0.63 (.427)	0.34 (.560)
Thanatophobia						
n (%)	6 (8.1)	6 (9.4)	9 (5.3)	1 (8.3)	3 (11.5)	3 (10.0)
χ^2 (*P*)	3.83 (.050)	3.98 (.046)	1.24 (.266)	0.82 (.365)	4.99 (.025)	3.77 (.052)
Functional somatic secondary symptoms						
n (%)	38 (51.3)	30 (46.9)	53 (31.0)	1 (8.3)	3 (11.5)	6 (20.0)
χ^2 (*P*)	63.58 (.000)	30.71 (.000)	28.07 (.000)	0.42 (.519)	0.24 (.624)	0.62 (.432)
Persistent somatization						
n (%)	15 (20.3)	16 (25.0)	43 (25.1)	1 (8.3)	3 (11.5)	2 (6.7)
χ^2 (*P*)	3.77 (.052)	5.55 (.018)	27.68 (.000)	0.21 (.645)	0.04 (.851)	1.02 (.313)
Conversion symptoms						
n (%)	4 (5.4)	5 (7.8)	7 (4.1)	0 (0)	0 (0)	0 (0)
χ^2 (*P*)	0.31 (.578)	1.40 (.236)	0.02 (.968)	0.42 (.518)	0.92 (.340)	1.05 (.304)
Anniversary reaction						
n (%)	5 (6.8)	7 (10.9)	10 (5.8)	0 (0)	0 (0)	2 (6.7)
χ^2 (*P*)	2.80 (.094)	9.23 (.002)	4.08 (.043)	0.30 (.583)	0.66 (.417)	2.30 (.129)
Type A behavior						
n (%)	19 (25.7)	18 (28.1)	44 (25.7)	2 (16.7)	10 (38.5)	6 (20.0)
χ^2 (*P*)	3.96 (.047)	3.02 (.082)	11.22 (.001)	0.01 (.917)	10.53 (.001)	0.46 (.500)
Irritable mood						
n (%)	31 (41.9)	32 (50.0)	62 (36.3)	3 (25.0)	13 (50.0)	6 (20.0)
χ^2 (*P*)	19.52 (.000)	20.02 (.000)	28.00 (.000)	0.12 (.734)	13.37 (.000)	0.02 (.899)
Demoralization						
n (%)	21 (28.4)	28 (43.7)	44 (25.7)	5 (41.7)	14 (53.8)	12 (40.0)
χ^2 (*P*)	0.65 (.421)	7.94 (.005)	0.39 (.530)	2.09 (.148)	13.02 (.000)	4.35 (.037)
Alexithymia						
n (%)	12 (16.2)	15 (23.4)	16 (9.4)	2 (16.7)	3 (11.5)	3 (10.0)
χ^2 (*P*)	0.77 (.380)	4.00 (.046)	1.75 (.186)	0.24 (.622)	0.01 (.935)	0.12 (.727)

[a]The percentages refer to the prevalence of each DCPR diagnosis within each specific anxiety disorder, while the χ^2 analysis is based on the whole sample of 1,660 patients that were compared in a 2 × 2 table with or without the specific anxiety disorder and with or without the specific DCPR disorder.
[b]In 2 patients with panic disorder with agoraphobia, DCPR evaluation was missing.
[c]In 11 patients with agoraphobia without history of panic disorder, DCPR evaluation was missing.
Abbreviation: DCPR = Diagnostic Criteria for Psychosomatic Research.

panic), provides evidence to the contrary in the medically ill and also some explanations for the occurrence of this discrepancy in clinical studies.

There is extensive literature, reviewed in detail elsewhere,[13] on the fact that patients with panic disorder and agoraphobia display significantly more hypochondriacal fears and beliefs compared to healthy subjects. Indeed, we also found significant associations with the DCPR syndromes of health anxiety and disease phobia in our sample. However, patients with agoraphobia without history of panic attacks displayed a highly significant association with illness denial. Persistent denial of having a medical disorder and needing treatment (eg, lack of compliance, delay in seeking medical attention) frequently occurs in the medical setting.[2,14,15] If

panic attacks have not taken place, agoraphobic fears tend to be "very refined and subtle, appear natural to the individual (and even part of his or her character) and are often highly rationalized."[16(p560)] It is only when a review of the patient's behavior is performed and exposure to phobic avoidances is encouraged[17] that "these patients become aware that their avoidances are not natural or inevitable."[16(p560)] Not surprisingly, there were no diagnoses of agoraphobia without panic attacks in the setting of consultation-liaison psychiatry, whereas panic disorder accounted for about 7% of diagnoses. Further, in our sample, agoraphobia without panic was also significantly related to the poor insight into the role of psychological states in the production of somatic symptoms that occurs in DCPR persistent somatization (a clustering of functional symptoms involving different organ systems) and anniversary reactions (a special form of conversion related to anniversaries, such as when the patient reaches the age of a parent who died).[2] Our findings thus suggest that agoraphobic fears, unlike panic attacks, do not tend to lead individuals to seek medical attention, even though they are associated with psychosomatic manifestations that impair quality of life.[6,15] The identification of these fears requires careful expert interviewing, well beyond the checklist use of diagnostic instruments,[8] to overcome the denial that underlies agoraphobia and other distress manifestations.

Indeed, the *DSM-V* Task Force core proposal for agoraphobia provides a better specification of the cluster of agoraphobic situations, such as being outside the home alone; using public transportation; being in open spaces; being in shops, theaters, or cinemas; standing in line; or being in a crowd.[9] A key clinical clue is the fact that mobility often requires the presence of a companion and/or should involve very familiar routes and places.[8]

Engel[18] outlined how feelings of helplessness and giving up may be associated with anniversaries. Indeed, demoralization, the consciousness of being unable to cope with a pressing problem or having failed to meet one's own expectations or those of others,[2,19] was found to characterize agoraphobia without history of panic disorder.

The findings thus support the view that agoraphobia should be conceptualized as an independent disease and not as simply a subordinate, residual form of panic disorder.[9]

The other diagnostic findings deserve brief comment. The overall prevalence rates of anxiety disorders that were found in our medical population exceeded those of epidemiologic studies performed in Italian general populations by clinicians.[20,21]

This particularly applies to panic disorder, agoraphobia without history of panic attacks, and generalized anxiety, whereas the other anxiety disturbances were within the expected ranges. Generalized anxiety disorder was the most frequent diagnosis (about 10% of cases), which is in line with the reported literature.[22] There were significant associations with somatization, abnormal illness behavior, Type A behavior, and irritable mood. The prevalence of social phobia (0.7%) in medical patients was lower than expected[22]: cases were limited to cardiology and dermatology.

While in specific settings (patients for whom consultation-liaison psychiatry was requested or frequent attenders of family practice) there might be an effect related to the type of population sample, it is difficult to explain the lack of cases in gastroenterology, endocrinology, and oncology. However, a recent survey of anxiety disorders in psychosomatic inpatients[23] also suggested that social phobia was comparatively rare. The low number of subjects with social anxiety in our investigation might explain the lack of significant correlations with psychosomatic variables.

Obsessive-compulsive disorder (1.6%) was related to dimensions of abnormal illness behavior, such as disease phobia and thanatophobia, as previously reported in psychiatric settings.[13] Type A behavior, irritable mood, and demoralization were also associated with obsessive-compulsive disorder.

The results of the present investigation thus indicate that anxiety disorders have important clinical implications in the setting of medical disease, as previously reported.[1] In view of the methodology that was used for assessing patients' psychosomatic manifestations based on DCPR,[2] the findings offer new insights into the characteristics of these manifestations. In particular, the results should alert physicians who are confronted with illness denial to look for symptoms related to agoraphobic avoidance. The clinical usefulness of incorporating DCPR criteria in the psychological assessment of the medically ill[5,6,24] is also supported.

In our sample, agoraphobia without history of panic disorder was found to be as common as panic disorder with agoraphobia. This provides full justification for retaining the diagnosis of agoraphobia in future diagnostic developments.[8,9]

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