Eur Arch Psychiatry Clin Neurosci (1994) 244:39–44

ORIGINAL PAPER

Gabriele Scheibe · Margot Albus

Prospective follow-up study lasting 2 years in patients with panic disorder with and without depressive disorders

Received: 6 September 1993 / Accepted: 23 February 1994

Summary A group of 52 patients presenting at an outpatient unit for anxiety disorders were included consecutively in a prospective 2-year follow-up study. Patients were administered to a structured interview for DSM-III-R diagnoses, a follow-up interview (LIFE), and various other ratings. Sociodemographic and illness-history characteristics, levels of anxiety and depressive symptoms, as well as psychosocial impairment, were evaluated at baseline and follow-up and compared between patients with panic disorder only and patients with panic disorder and concomitant depressive disorders at index assessment. Cross-sectional and longitudinal differences between patients with panic disorder only and patients with panic disorder and concomitant depression have been found, indicating that patients with comorbid conditions are more severely ill and have a less favorable outcome. For the total sample, however, the 2-year outcome was better than that reported in many other follow-up studies.

Key words Panic disorder · Depression · Comorbidity Structured interview (SCID; LIFE)

Introduction

Prospective long-term follow-up studies comparing panic disorder with and without depressive disorders are rare. The majority of follow-up studies reported so far were carried out prior to the introduction of DSM-III or were retrospective in design (Uhde et al. 1985; Breier et al. 1986; Noyes et al. 1989). This implies difficulties in comparing the results because of differences in diagnostic criteria and the bias of inaccurate retrospective reporting. Prospective clinical studies in patients with panic disorder and depressive disorders were caried out by Buller et al. (1986), Maier and Buller (1988), Nagy et al. (1989), Noyes et al. (1990), and Wittchen et al. (1991), and prospective epidemiological studies were carried out by Vollrath and Angst (1989) and Vollrath et al. (1990). Thus far, clinical studies show equivocal results: Although the data of Maier and Buller (1988) argue for a rather favorable outcome of panic disorder and agoraphobia, other authors (Breier et al. 1986; Krieg et al. 1987; Noyes et al. 1990; Wittchen et al. 1991) report a chronic course of panic, anxiety, and phobias. Therefore, differences in patient referral sources, inclusion and exclusion criteria, diagnostic systems and instruments, treatment settings, and study design might influence the outcome data in these investigations (Leckman et al. 1984; Rubin and Lesser 1990; Albus and Scheibe 1993).

Patients with anxiety disorders and concomitant depression are reported to be more severely ill by a number of studies (Van Valkenburg et al. 1984; Charney et al. 1986; Buller et al. 1986; Reich 1988; Stein and Uhde 1988; Vollrath and Angst 1989). Moreover, patients with panic disorder only and patients with panic disorder and concomitant depression differ considerably with regard to subjective suffering (Vollrath and Angst 1989). Correspondingly, depression in panic disorder (Charney et al. 1986; Lesser et al. 1988, 1989; Maier et al. 1989; Nagy et al. 1989, Noyes et al. 1990) and other anxiety disorders (Barlow et al. 1986) were associated with an increased level of anxiety. In contrast, other authors have reported no effect (Buller et al. 1986; Argyle and Roth 1989) of depression on the severity of anxiety symptoms.

Severe avoidance behavior has been reported to be more prevalent in the depressed subgroup (Cassano et al. 1989; Noyes et al. 1990). Moreover, patients with comorbid conditions are reported to score higher on measures of depression (Barlow et al. 1986; Buller et al. 1986; Charney et al. 1986; Lesser et al. 1988, 1989; Cassano et al. 1989; Nagy et al. 1989) and measures of phobia (Cassano et al. 1989; Vollrath et al. 1990). Furthermore, in many studies panic patients with a history of depression show more severe psychosocial impairment or disability (Buller et al. 1986; Charney et al. 1986; Wittchen 1988; Lesser et al. 1988).

Margot Albus (✉) · Gabriele Scheibe
State Mental Hospital Haar, Vockestr. 72,
D-85529 Haar, Germany

There is evidence that patients with anxiety and depression have a less favorable outcome or a more chronic course than patients with anxiety disorders exclusively (Van Valkenburg et al. 1984; Wittchen 1988; Noyes et al. 1990; Angst and Vollrath 1991; Wittchen et al. 1991). Patients with comorbid conditions have been reported to have poorer psychosocial adjustment at outcome (Van Valkenburg et al. 1984; Wittchen 1988; Hecht et al. 1989), more symptom-related disability at follow-up (Noyes et al. 1990), lower recovery rates (Vollrath et al. 1990) and higher relapse rates (Reich 1988).

The present prospective follow-up study was designed to investigate if there are differences in patients with panic disorder with and without concomitant depression with regard to baseline ratings of severity of illness and subjective suffering, and if the outcome of patients with panic disorder is different compared to the outcome of patients with concomitant depression.

Patients and methods

A total of 89 subjects were recruited through news media and interviewed at the outpatient unit for anxiety disorders at the Psychiatric Hospital of the University of Munich. Of this sample 29 patients did not meet the inclusion criteria for the controlled-treatment study (i.e., age 18–60 years, no suicidal tendencies, no pregnancy or nursing, no obsessive–compulsive symptoms, no comorbidity with other anxiety disorders, such as generalized anxiety disorder, social phobia, or simple phobia, no history of physical illness that could explain their symptoms, and no alcohol or drug dependence. The other 60 patients met DSM-III-R criteria for panic disorder with or without agoraphobia, but 8 patients dropped out after refusing to participate in the initial controlled-drug-treatment study. The remaining 52 patients were included consecutively in the study.

After index assessment patients were enrolled in an 8-week controlled-treatment study of either imipramine or doxepin. Additionally, patients received supportive psychotherapy 1 h/week for 6–8 months, depending on their clinical status. Patients were thereafter treated naturalistically, including booster sessions. During these sessions symptoms of anxiety and depression, as well as phobic situations, were evaluated and instructions given for in vivo exposure. Psychotropic drugs were also prescribed. To evaluate fluctuations in anxiety and depressive symptoms, and to avoid the bias of inaccurate retrospective reporting, patients were rated at least every 3 months throughout the entire observation period. These data are reported in another paper (Albus and Scheibe 1993).

The Structured Clinical Interview for DSM-III-R (SCID; Spitzer et al. 1987), which provides current and lifetime DSM-III-R diagnoses, was administered to each subject by two clinicians (G.S. and M.A) who were experienced in using the DSM-III-R classification system and trained in applying the SCID. In a subsample of patients ($n = 30$) randomly selected from the sample investigated SCID diagnoses were evaluated independently by both clinicians, which turned out to be sufficient ($\kappa = 0.82$).

Patients were divided into two subgroups: panic patients without ($n = 32$) and with ($n = 20$) concomitant depression at baseline investigation. Of the 20 patients with concomitant depression, 10 patients met DSM-III-R criteria for major depression, 7 patients for dysthymic disorder, and 3 patients for major depression and dysthymic disorder. Of the comorbid group 10% reported a simultaneous onset of panic disorder and depression, 40% an earlier onset of depression, and 50% an earlier onset of panic disorder.

At follow-up patients were interviewed again using SCID and the Longitudinal Interval Follow-up Evaluation (LIFE) (Shapiro and Keller 1979; German translation by Paulus and Philipp 1986). The LIFE is a semistructured interview with quantitatively scaled items that assess detailed psychosocial (work, leisure, interpersonal relationships, sexual activities and satisfaction, and social adjustment) and therapeutic (nonpsychiatric medical illness, nonpsychiatric drugs, psychotropic drugs, and psychotherapy) information for the 6 months prior to follow-up. Furthermore, the overall level (range 1–100) of psychosocial adjustment by means of the Global Assessment Scale (GAS; Spitzer et al. 1976) for the previous 6 months was evaluated. Additionally, the following ratings were performed as clinicians' ratings at index assessment and

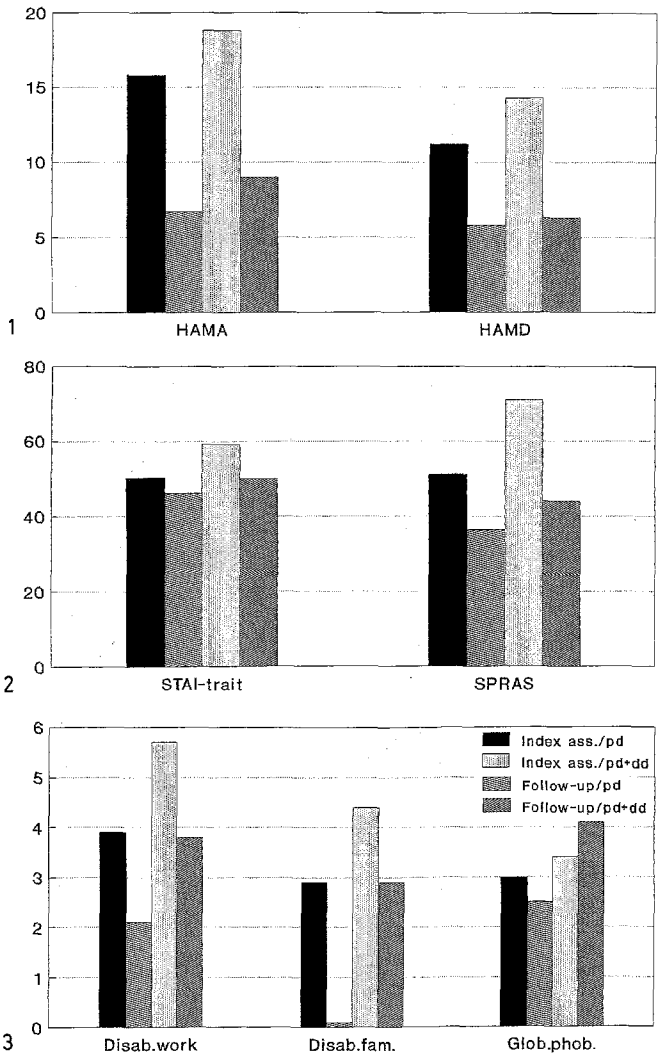

Fig. 1 Hamilton Anxiety Scale (HAMA) and Hamilton Depression Scale (HAMD) at baseline (*Index ass.*) and 2-year follow-up for patients with panic disorder only (*pd*) and patients with panic disorder and concomitant depression (*pd + dd*) at index assessment

Fig. 2 Trait Anxiety Inventory (*STAI-trait*) and Sheehan Patient-Rated Anxiety Scale (*SPRAS*) at baseline (*Index ass.*) and 2-year follow-up for patients with panic disorder only (*pd*) and patients with panic disorder and concomitant depression (*pd + dd*) at index assessment

Fig. 3 Work disability (*Disab. work*), Family Life Disability (*Disab. fam.*) and global phobia (*Glob. phob.*) at baseline (*index ass.*) and 2-year follow-up for patients with panic disorder alone (*pd*) and patients with panic disorder and concomitant depression (*pd + dd*) at index assessment

Table 1 Baseline demographic and illness characteristics of patients with panic disorder (pd) with and without concomitant depression at index assessment

	Panic disorder (n = 32) %	Panic disorder and depression (n = 20) %	χ^2 test		
Gender			n.s.		
Male	40.6	30.0			
Female	59.4	70.0			
Marital status			n.s.		
Never married	21.9	36.8			
Married	68.8	57.9			
Separated, divorced	9.4	5.3			
	Mean ± SD	Mean ± SD	Student's t-test		
			t	df	P
Age at admission	40.4 ± 6.9	34.8 ± 6.9	2.80	50	0.01
Duration of illness (years)	6.0 ± 5.6	10.8 ± 9.3	−2.33	50	0.02
Age at onset of panic disorder	32.7 ± 9.1	28.1 ± 10.2	2.32	50	0.01
Age at onset of avoidance behavior	32.9 ± 8.6	27.6 ± 9.9	2.45	50	0.01
Age at onset of first depressive episode	–	24.0 ± 10.3		–	

at 2-year follow-up: Hamilton Anxiety Scale (range 0–56) (HAMA; Hamilton 1959; see Fig. 1), Hamilton Depression Scale (range 0–67) (HAMD; Hamilton 1967; see Fig. 1), Phobia Scale (range of global phobia 0–10; Marks and Matthews 1979), and Disability Scales on work, social life/leisure, and family/homelife impairment (Cross-National Collaborative Panic Study 1992; see Fig. 3) rated from 0 = no impairment to 10 = total impairment. State-Trait Anxiety Inventory (STAI; range 0–80; Spielberger et al. 1970; see Fig. 2) and Sheehan Patient-Rated Anxiety Scale (SPRAS; range 0–184; Sheehan 1986; see Fig. 2) were performed as patients' ratings.

Statistical analysis employed nonparametric χ^2 tests for determining significance of categorical data and two-tailed t-tests for independent samples to test for the significance of differences between continuous variables.

Results

Baseline characteristics

Subjects included in the present study were predominantly women, especially in the comorbid group. Concerning marital status there were no significant differences between the groups. Patients with comorbid conditions had an earlier age at admission, age at onset of panic disorder, and age at onset of avoidance behavior, as well as a significantly longer duration of illness, than patients with panic disorder only (Table 1).

The primary DSM-III-R diagnoses were distributed as follows: panic disorder with agoraphobia in 39 cases (14 with concomitant depression) and panic disorder without agoraphobia in 13 cases (6 with concomitant depression).

Severity of illness at index assessment and at 2-year follow-up

Considering the baseline ratings it is obvious that patients with panic and concomitant depression were more severely ill at index assessment. They had significantly higher scores on most scales that included both clinicians' and patients' ratings. Patients of the comorbid group showed higher baseline levels of anxiety and depression, as well as a more severe disability in work and family life, than subjects without depression.

At 2-year follow-up patients with concomitant depression at index assessment show more severe global phobia and more severe impairment in work and family life compared to patients with panic only (Fig. 3). According to self- and observer-rated levels of anxiety and depression, no significant differences could be further established.

Diagnostic and clinical evaluation at 2-year follow-up

Concerning treatment during the past 6 months before follow-up assessment, there were no significant differences between the two groups: Patients with panic disorder had sought help from therapeutic sessions and had used psychotropic drugs during the past 6 months approximately as much as patients with panic and concomitant depression (Table 2).

Analyzing the psychosocial 2-year follow-up data (LIFE), the following significant difference was found: Patients with panic disorder only reported better partner relationships and more sexual activity than patients of the comorbid group. No significant differences occurred in the other psychosocial areas evaluated with the LIFE interview. Concerning the GAS significant differences be-

Table 2 Status at the end of the 2-year follow-up of patients with panic disorder only and patients with panic disorder and depression at index assessment. Remitted was defined as the patient not meeting the DSM-III-R criteria for anxiety disorders or depressive disorders. GAS Global Assessment Scale

	Panic disorder (n = 32)	Panic disorder and depression (n = 20)	χ^2 test		
	%	%	χ^2	df	P
Psychotherapeutic sessions	62.5	60.0			
Psychotropic drugs during past 6 months	43.7	40.0	n.s.		
Antidepressives	18.5	15.0			
Antidepressives + benzodiazepine	9.4	5.0			
Antidepressives + betablockers	6.5	10.0			
Benzodiazepine ad lib.	9.3	10.0			
Partner relationships during past 6 months			5.99	2	0.05
Good	71.0	36.8			
Moderate	19.4	21.1			
Poor	9.6	42.1			
Frequency of sexual activity during past month			7.31	2	0.02
>1–3 times/week	74.1	37.5			
>once/month	7.4	37.5			
Rarely/never	18.5	25.0			
Status of follow-up			11.67	2	0.01
Remitted	75.0	35.0			
Unremitted	25.0	65.0			
	Mean ± SD	Mean ± SD	Student's t-test		
			t	df	P
GAS	80.7 ± 9.8	74.0 ± 12.8	2.06	50	0.05
Remitted patients					
Phobic fears	9.4 ± 9.1	12.2 ± 2.7	n.s.		
Phobic avoidance	4.3 ± 4.3	3.7 ± 0.5	n.s.		
Unremitted patients					
Phobic fears	14.2 ± 8.6	19.7 ± 8.1	n.s.		
Phobic avoidance	6.0 ± 2.3	5.5 ± 5.1	n.s.		

tween the groups occurred for the past 6 months: Patients of the pure panic group showed better psychosocial functioning than patients of the comorbid group (Table 2).

In contrast to 35% of the comorbid group, 75% of the patients with panic only were remitted e.g., did not meet the DSM-III-R criteria at follow-up, neither for anxiety disorders, nor depressive disorders. Patients remitted at follow-up in the pure panic group and the comorbid group still reported phobic fears and phobic avoidance at 2-year follow-up, although to a nonsignificant degree compared to unremitted patients. In contrast to 9.4% of the panic patients, 45% of the comorbid patients showed continuous symptoms of the illness throughout the entire observation period. The recurrence rates of anxiety and/or depressive disorders were similar in both groups. These data are reported elsewhere (Albus and Scheibe 1993).

Discussion

A greater severity of illness has been found in the panic group with concomitant depression compared to the pure panic group with regard to levels of anxiety, depression, and disability at index assessment. This finding agrees with most clinical and epidemiological studies (Van Valkenburg et al. 1984; Barlow et al. 1986; Buller et al. 1986; Charney et al. 1986; Lesser et al. 1988, 1989; Reich 1988; Stein and Uhde 1988; Wittchen 1988; Cassano et al. 1989; Hecht et al. 1989; Maier et al. 1989; Nagy et al. 1989; Vollrath and Angst 1989; Noyes et al. 1990; Vollrath et al. 1990) and supports the hypothesis that patients with comorbid conditions are more severely ill. Additionally, the higher scores in the self-ratings (STAI-trait and SPRAS) indicate a more severe subjective suffering of these patients. One might assume that the longer duration of illness or the older age at index of the comorbid group have confounded the results. However, neither age nor duration of illness showed any significant effects (Albus and Scheibe 1993).

According to the 2-year follow-up data the outcome of patients with concomitant depression was less favorable, which is in accordance with various other studies (Van Valkenburg et al. 1984; Wittchen 1988; Nagy et al. 1989; Noyes et al. 1990; Angst and Vollrath 1991; Wittchen et al. 1991). Worse relationships and more impairment of psychosocial functioning of the dual-diagnosis group have been reported by several authors (Wittchen 1988; Hecht et al. 1989). The data suggest that the successful treatment of panic attacks or symptoms related to anxiety only is not a sufficient outcome goal (Nagy et al. 1989).

These results indicate that comorbidity of panic disorder and depressive disorders seems to have important diagnostic, prognostic, and treatment implications. In accordance with other prospective follow-up studies (Maier and Buller 1988; Nagy et al. 1989; Noyes et al. 1990), the patient-sample investigated in this study shows a better outcome than reported in retrospective studies (Breier et al. 1986; Krieg et al. 1987). However, the different definitions of outcome used in these studies renders comparison difficult. Noyes et al. (1990) reported that 10% of their panic patients had no anxiety symptoms at 3-year follow-up. Maier and Buller (1988) and Nagy et al. (1989) found 43–48% of patients with panic disorder with or without agoraphobia to be syndrome-free or remitted at follow-up, without further specifying their findings.

In our study 75% of patients with panic disorder only and 35% of patients with panic and concomitant depression were remitted (e.g., did not meet the criteria for a DSM-III-R diagnosis of anxiety disorders or depressive disorders. This finding supports the assumption that patients with comorbid conditions tend to develop a more chronic course, and agrees with the results of other studies (Noyes et al. 1990; Wittchen et al. 1991).

Focusing on a global outcome measure such as the GAS (Spitzer et al. 1976), the patients investigated in this study scored a mean of 80 and 74, respectively, which reflects only slight overall impairment. This finding is in accordance with Noyes et al. (1990), whose patients scored a mean of 72. These data emphasize that the overall outcome of panic disorder patients with or without concomitant depression is more favorable than reported in retrospective studies.

The divergent results of naturalistic treatment studies in patients with anxiety disorders may be attributable to differences in the samples investigated. The data suggest that outpatients who have been recruited via media news (such as our sample) or have been recruited from nonpsychiatric settings (Maier and Buller 1988) show a more favorable outcome than patients who were already hospitalized (Krieg et al. 1987; Coryell et al. 1983; Wittchen et al. 1991) or patients recruited at psychiatric treatment sites (Breier et al. 1986). Patients who were recruited from nonpsychiatric settings tend to have milder illnesses than those recruited from treatment facilities (Noyes et al. 1989), which may contribute to a more favorable outcome.

Besides the significantly lower remission rates of the comorbid sample and more severe impairment in work and family life, the comorbid group showed worse partner relationships and less sexual activity compared to the pure panic group. This area has not yet been considered by follow-up studies in patients with anxiety with and without concomitant depression.

In summary, the patient-sample investigated in this study showed a considerably better outcome than those in many other follow-up studies. Besides the possibility that this sample suffers from milder illnesses than patients recruited from psychiatric settings, it may be assumed that a therapeutic regimen with an initially controlled treatment period, followed by either antipanic medication or psychotherapy (including booster sessions), has prevented mainly patients with panic disorder only from developing persistent and disabling symptoms as reported in other studies.

References

Albus M, Scheibe G (1993) Outcome of panic disorder with or without concomitant depression. A two-year prospective follow-up study. Am J Psychiatry 150:1878–1880

American Psychiatric Association (1987) Diagnostic and Statistical Manual of Mental Disorders, 3rd edn, revised (DSM-III-R). American Psychiatric Association, Washington DC

Angst J, Vollrath M (1991) The natural history of anxiety disorders. Acta Psychiatr Scand 84:446–452

Argyle N, Roth M (1989) The phenomenological study of 90 patients with panic disorder. Psychiatr Dev 3:187–209

Barlow DH, DiNardo PA, Vermilyea BB, Vermilyea J, Blanchard EB (1986) Co-morbidity and depression among the anxiety disorders. Issues in diagnosis and classification. J Nerv Ment Dis 174:63–72

Breier A, Charney DS, Heninger GR (1986) Agoraphobia with panic attacks: development, diagnostic stability, and course of illness. Arch Gen Psychiatry 43:1029–1036

Buller R, Maier W, Benkert O (1986) Clinical subtypes in panic disorder. Their descriptive and prospective validity. J Affect Disord 11:105–114

Cassano GB, Perugi G, Musetti L, Akishkal HS (1989) The nature of depression presenting concomitantly with panic disorder. Compr Psychiatry 30:473–482

Charney DS, Heninger GR, Price LH, Breier A (1986) Major depression and panic disorder. Diagnostic and neurobiological relationships. Psychopharmacol Bull 22:503–511

Cross-National Collaborative Panic Study, Second Phase Investigators (1992) Drug treatment of panic disorder: comparative efficacy of alprazolam, imipramine, and placebo. Br J Psychiatry 160:191–202

Hamilton MA (1959) The assessment of anxiety states by rating. Br J Med Psychol 32:50–55

Hamilton MA (1967) Development of a rating scale for primary depressive illness. Br J Clin Psychol 6:278–296

Hecht H, Zerrsen D v, Krieg JC, Pössl J, Wittchen H-U (1989) Anxiety and depression: comorbidity, psychopathology, and social functioning. Compr Psychiatry 30:420–433

Krieg JC, Bronisch T, Wittchen H-U, Zerssen D v (1987) Anxiety disorders: a long-term prospective and retrospective follow-up study of former inpatients suffering from an anxiety neurosis or phobia. Acta Psychiatr Scand 76:36–47

Leckman JF, Weissman MM, Merikangas KR, Pauls DL, Prusoff BA (1984) Methodologic differences in major depression and panic studies. Arch Gen Psychiatry 41:722–723

Lesser IM, Rubin RT, Pecknold JC, Rifkin A, Swinson RP, Lydiard RB, Ballenger JC, Burrows GD, Noyes R, DuPont RL (1988) Secondary depression in panic disorder and agorapho-

bia. Part I: frequency, severity, and response to treatment. Arch Gen Psychiatry 45:437–443
Lesser IM, Rubin RT, Rifkin A, Swinson RP, Ballenger JC, Burrows GD, Dupont RL, Noyes R, Pecknold JC (1989) Secondary depression in panic disorder and agoraphobia. Part II: dimensions of depressive symptomatology and their response to treatment. J Affect Disord 16:49–58
Maier W, Buller R (1988) One-year follow-up of panic disorder. Eur Arch Psychiatry Neurol Sci 238:105–109
Maier W, Rosenberg R, Argyle N, Buller R, Roth M, Brandon S, Benkert O (1989) Avoidance behaviour and major depression in panic disorder: a report from the Cross-National Collaborative Panic Study. Psychiatr Dev 2:123–142
Marks IM, Matthews AM (1979) Brief standard self-rating for phobic patients. Behav Res Ther 17:263–267
Nagy LM, Krystal JH, Woods SW, Charney DS (1989) Clinical and medication outcome after short-term alprazolam and behavioral group treatment in panic disorder. Arch Gen Psychiatry 46:993–999
Noyes R, Garvey MJ, Cook BL (1989) Follow-up study of patients with panic disorder and agoraphobia with panic attacks treated with tricyclic antidepressants. J Affect Disord 16:249–257
Noyes R, Reich J, Christiansen J, Suelzer M, Pfohl B, Coryell WA (1990) Outcome of panic disorder: relationship to diagnostic subtypes and comorbidity. Arch Gen Psychiatry 47:809–818
Paulus M, Philipp M (1986) Longitudinal Interval Follow-up Evaluation (LIFE). German translation, version 1.1, Mainz, Germany
Reich J (1988) DSM-III personality disorders and the outcome of treated panic disorder. Am J Psychiatry 145:1149–1152
Rubin RT, Lesser JM (1990) Secondary depression in panic patients. J Psychiatr Res 24 (suppl.1):78–79
Shapiro R, Keller M (1979) Longitudinal Interval Follow-up Evaluation (LIFE). Massachusetts General Hospital, Boston, Mass.
Spielberger CD, Gorsuch RC, Lushene RF (1970) Manual for the State-Trait Anxiety Inventory. Consulting Psychologists Press, Palo Alto, Calif.
Spitzer RL, Gibbon M, Endicott J, Fleiss JL, Cohen J (1976) The Global Assessment Scale: a procedure for measuring overall severity of psychiatric disturbance. Arch Gen Psychiatry 33:766–771
Spitzer RL, Williams JBW, Gibbon M (1987) Structured Clinical Interview for DSM-III-R (SCID). Biometrics Research Department, New York State Psychiatric Institute, New York
Stein MB; Uhde TW (1988) Panic disorder and major depression: a tale of two syndromes. Psychiatr Clin North Am 11:441–461
Uhde TW, Boulenger JP, Roy-Byrne PP, Geraci MF, Vittone BJ, Post RM (1985) Longitudinal course of panic disorder: clinical and biological considerations. Prog Neuropsychopharmacol Biol Psychiatry 9:39–51
Valkenburg C van, Akiskal HS, Puzantian V, Rosenthal T (1984) Anxious depressions: clinical, family history, and naturalistic outcome – comparisons with panic and major depressive disorders. J Affect Disord 6:67–82
Vollrath M, Angst J (1989) Outcome of panic and depression in a seven-year follow-up study: results of the Zurich Study. Acta Psychiatr Scand 80:591–596
Vollrath M, Koch R, Angst J (1990) The Zurich study IX. Panic disorder and sporadic panic: symptoms, diagnosis, prevalence, and overlap with depression. Eur Arch Psychiatry, Neurol Sci 239:221–230
Wittchen H-U (1988) Natural course and spontaneous remissions of untreated anxiety disorders: results of the Munich Follow-up Study (MFS). In: Hand I, Wittchen H-U (eds) Panic and phobias 2. Springer, Berlin Heidelberg New York, pp 3–17
Wittchen H-U, Essan CA, Krieg J-C (1991) Anxiety disorders: similarities and differences of comorbidity in treated and untreated groups. Br J Psychiatry 159 (suppl. 12):23–33