Social Anxiety Disorder Clinical Course and Outcome: Review of Harvard/Brown Anxiety Research Project (HARP) Findings

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Preliminary findings from a long-term, prospective, longitudinal, naturalistic treatment study of adults with social anxiety disorder (SAD) demonstrate that this illness has a chronic course and a greater adverse impact on social functioning than do depressive symptoms or chronic medical illnesses. Comorbid anxiety, depressive, and personality disorders are common in patients with SAD. Only 35% of patients with SAD recovered after 10 years of prospective follow-up. Whereas, the relapse rate, once recovery is achieved, is 34% during this 10-year follow-up. Treatment is underutilized in patients with SAD, and a long-term treatment approach may be needed to improve the likelihood of recovery from SAD. *(J Clin Psychiatry 2006;67[suppl 12]:14–19)*

Social anxiety disorder (SAD) is a common illness characterized by excessive concern about situations in which one might be subject to the scrutiny of others and appear anxious or have an inordinate fear that one's actions or words might appear foolish or embarrassing. The illness has an early age at onset, a chronic course, and a pervasive detrimental impact on social and occupational functioning. Data collected in the Harvard/Brown Anxiety Research Project (HARP), an ongoing long-term, prospective, longitudinal, naturalistic treatment study of adults with DSM-III-R anxiety disorders, provide additional insight into the clinical course and outcome in patients with SAD.[1]

STUDY DESIGN AND METHODOLOGY

Subjects with at least 1 past or current episode of 1 or more DSM-III-R anxiety disorders (e.g., SAD, panic disorder with or without agoraphobia, or generalized anxiety disorder) were referred for the study by the investigators in their private practices, physicians at site hospital psychiatric clinics, or primary care physicians working at site hospitals.[1] Enrollment of subjects began in 1989.[2] A total of 711 subjects have been followed at 6-month or 1-year intervals for at least 13 years, with a goal of 16 to 18 years of follow-up.[1]Assessment methods have been described previously.[2] Standardized interviewing methods and operational definitions and measures were used, with multiple domains for outcomes. The prospective design, long study duration, large sample size, and short follow-up intervals are strengths of the study.

SUBJECT CHARACTERISTICS

The most common index episode diagnoses (Table 1) were panic disorder (50% with agoraphobia and 12% without agoraphobia), major depressive episode (27%), SAD (25%), and generalized anxiety disorder (25%).[1] The characteristics of the subjects with SAD, panic disorder with or without agoraphobia, or generalized anxiety disorder (GAD) are shown in Table 2. The subjects were primarily white. Efforts began in the fall of 2004 to recruit a cohort of 200 Hispanics and African Americans with anxiety disorders.

The demographic data were similar for subjects with SAD, panic disorder with or without agoraphobia, and GAD (M.B.K., unpublished data, 2003). The age at onset of the illness was lower for SAD than panic disorder with or without agoraphobia or GAD, but the level of education did not differ (a lower education level might have been anticipated in subjects with SAD because of the earlier onset of illness). Occupational functioning was similar among the 4 illnesses.

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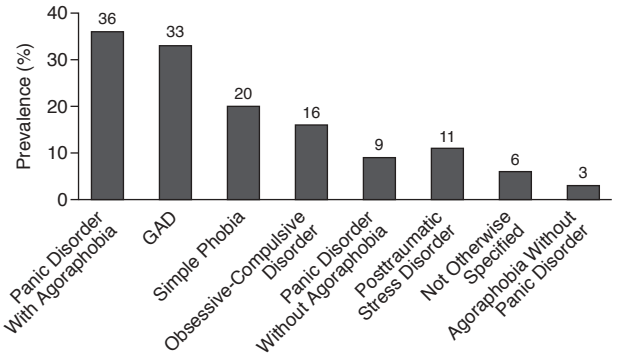
Table 1. Index Episode Diagnosis in HARP Sample (N = 711)[a]

Index Episode Diagnosis	N (%)[b]
Uncomplicated panic disorder without agoraphobia	82 (12)
Panic disorder with agoraphobia	357 (50)
Agoraphobia without panic disorder	30 (4)
Generalized anxiety disorder	179 (25)
Social anxiety disorder	176 (25)
Simple phobia	115 (16)
Posttraumatic stress disorder	56 (8)
Obsessive-compulsive disorder	113 (16)
Anxiety not otherwise specified	59 (8)
Major depressive episode	190 (27)

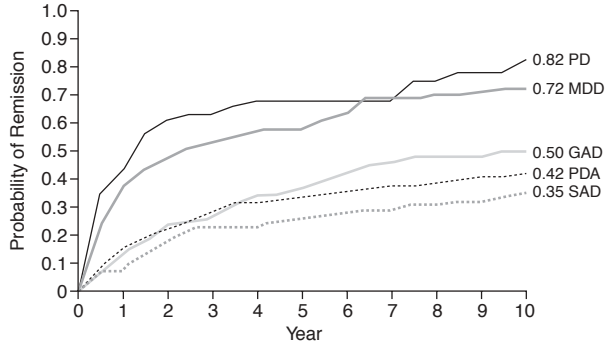
[a]Data from Dyck et al.[1]
[b]The percentage figures do not add up to 100 because the diagnoses were not mutually exclusive.
Abbreviation: HARP = Harvard/Brown Anxiety Research Project.

Figure 1. Prevalence of Selected Comorbid Conditions at Time of Intake in HARP Study Subjects With Social Anxiety Disorder (N = 176)[a]



[a]M. B. Keller, M.D., unpublished data, 2002.
Abbreviations: GAD = generalized anxiety disorder, HARP = Harvard/Brown Anxiety Research Project.

Figure 2. Cumulative Recovery Rate in HARP Study Subjects With Anxiety Disorders or Major Depressive Disorder[a]



[a]M. B. Keller, M.D., unpublished data, 2004.
Abbreviations: GAD = generalized anxiety disorder, HARP = Harvard/Brown Anxiety Research Project, MDD = major depressive disorder, PD = panic disorder without agoraphobia, PDA = panic disorder with agoraphobia, SAD = social anxiety disorder.

All 4 anxiety disorders had a negative impact on social functioning that was greater than that of depressive symptoms.[1] Depressive symptoms have been shown to have a significantly greater adverse impact on social functioning than certain chronic medical conditions (e.g., diabetes mellitus, advanced coronary artery disease, hypertension, arthritis, lung problems, back problems, gastrointestinal problems).[3]

COMORBID CONDITIONS

Comorbid anxiety disorders were common at the time of intake in subjects with SAD, panic disorder with or without agoraphobia, and GAD (Table 3). Subjects with SAD or GAD were more likely than subjects with panic disorder with or without agoraphobia to have comorbid anxiety disorders.[1]

The types of comorbid conditions at the time of intake in the 176 subjects with SAD are shown in Figure 1. Panic disorder with agoraphobia and GAD were the most common comorbid conditions in subjects with SAD (i.e., there was considerable overlap in presentation of these anxiety disorders).

At any given time over the course of follow-up, the predominant anxiety disorder typically was different than the one associated with the index episode. The likelihood of this "morphing" of the phenotype was at least 50%. The rate of change in phenotype was comparable among the 4 anxiety disorders, despite expectations that SAD would be more stable than the other anxiety disorders (M.B.K, unpublished data, 2003). The etiology and pathogenesis of these changes remain to be studied.

Comorbid depressive disorders at the time of intake were common in subjects with SAD, panic disorder with or without agoraphobia, or GAD (Table 4). About half of subjects with these anxiety disorders had a comorbid depressive disorder. Subjects with SAD and comorbid major depression at the time of intake were more likely to have additional comorbid anxiety disorders, a history of psychiatric hospitalization, a lower socioeconomic and educational status, significant disability in most areas of social functioning, and lower quality-of-life functioning than subjects without comorbid major depression.[4]

The prevalence of comorbid personality disorders was higher in subjects with SAD than in subjects with panic disorder with or without agoraphobia or GAD at the time of intake (Table 5).[1] The difference is largely the result of a significantly greater prevalence of personality disorder in subjects with SAD than in subjects with 1 of the other 3 anxiety disorders.[1]

RECOVERY AND REMISSION

In the past, the terms *recovery* and *remission* were used interchangeably for patients with SAD; the terms were

Table 2. Subject Characteristics in HARP Study[a]

Characteristic	Social Anxiety Disorder (N = 176)	Panic Disorder With Agoraphobia (N = 357)	Panic Disorder Without Agoraphobia (N = 82)	Generalized Anxiety Disorder (N = 179)
Sex, %				
Male	40	31	45	29
Female	60	69	55	71
Partner status, %				
Married/with significant other	51	59	52	56
Divorced, widowed, or separated	15	15	17	15
Never married	34	26	31	29
Age at intake, mean, y	39	40	40	41
Education, %				
Attended or graduated from graduate school	15	14	16	15
Graduated from college	20	21	24	22
Attended college	30	30	31	29
Graduated from high school	25	26	26	28
Did not graduate from high school	9	9	4	6
Working full-time, %	47	42	52	45
Receiving public assistance,[b] %	22	25	22	26
Unemployment compensation, %	5	5	6	3
Disability payments, %	5	14	11	15
Social security payments, %	6	9	5	8
Welfare payments, %	5	2	4	3
Length of intake episode, mean, y	18.0	16.6	11.0	18.1
Age at onset of illness, mean, y	14.4	27.1	34.4	21.3
Global assessment at intake,[c] mean, score	57	59	59	57

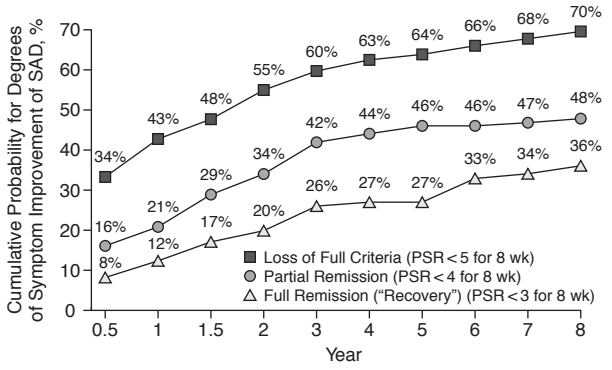
[a]M. B. Keller, M.D., unpublished data, 2003.
[b]Public assistance includes unemployment compensation, disability payments, social security payments, and welfare payments.
[c]A global assessment score of 51–60 indicates moderate symptoms or moderate difficulty with social or occupational functioning.
Abbreviation: HARP = Harvard/Brown Anxiety Research Project.

Table 3. Prevalence (%) of Comorbid Anxiety Disorders at the Time of Intake in HARP Study Subjects With Social Anxiety Disorder, Panic Disorder With and Without Agoraphobia, or Generalized Anxiety Disorder[a]

Number of Comorbid Anxiety Disorders at Intake	Social Anxiety Disorder (N = 176)	Panic Disorder With Agoraphobia (N = 357)	Panic Disorder Without Agoraphobia (N = 82)	Generalized Anxiety Disorder (N = 179)
0	24	57	56	18
1	44	27	29	45
> 1	32	16	15	37

[a]M. B. Keller, M.D., unpublished data, 2002.
Abbreviation: HARP = Harvard/Brown Anxiety Research Project.

Figure 3. Cumulative Probability of 3 Different Degrees of Symptom Improvement in HARP Study Subjects With Social Anxiety Disorder[a]



[a]M. B. Keller, M.D., unpublished data, 2003.
Abbreviations: HARP = Harvard/Brown Anxiety Research Project, PSR = Psychiatric Status Rating, SAD = social anxiety disorder.

defined as returning to one's usual self or having only 1 or 2 mild symptoms of the disorder for at least 8 consecutive weeks. A psychiatric status scale for SAD[5] is now used to quantify symptom improvement, and different degrees of symptom improvement may be used as outcome measures. In the HARP study, a *recovery* was defined as *remission*, with the designations *partial remission* and *loss of full criteria* reserved for lesser improvement in symptoms. The cumulative remission rate over a 10-year period (Figure 2) was lower for subjects with SAD (35%) than subjects with panic disorder with agoraphobia (42%), GAD (50%), major depressive disorder (72%), and panic disorder without agoraphobia (82%) (M.B.K., unpublished data, 2004). The cumulative probabilities of partial remission and loss of full criteria in subjects with SAD over an 8-year period (48% and 70%, respectively) were higher than the cumulative probability of full remission of SAD (Figure 3) (M.B.K., unpublished data, 2003).

Table 4. Prevalence (%) of Comorbid Depressive Disorders at the Time of Intake in HARP Study Subjects With Social Anxiety Disorder, Panic Disorder With and Without Agoraphobia, or Generalized Anxiety Disorder[a]

Type of Disorder	Social Anxiety Disorder (N = 176)	Panic Disorder With Agoraphobia (N = 357)	Panic Disorder Without Agoraphobia (N = 82)	Generalized Anxiety Disorder (N = 179)
Any depressive disorder[b]	56	42	49	58
Major depression	35	25	33	39
Dysthymia	23	15	15	18
Minor depression	4	6	2	5
Double depression[c]	6	4	0	4

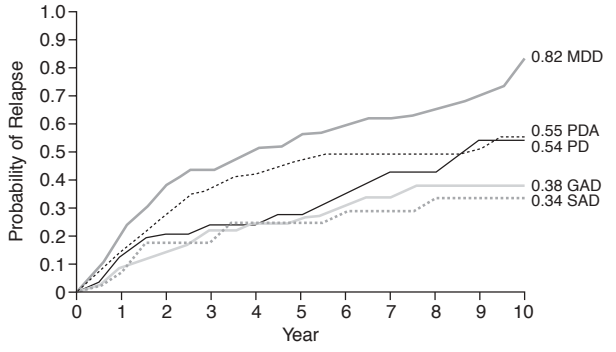
[a]Data from Keller.[4]
[b]Some subjects had multiple depressive disorders, so the percentage figures for specific disorders may add up to more than the total for "Any depressive disorder."
[c]Double depression is defined as both major depression and dysthymia at the time of intake.
Abbreviation: HARP = Harvard/Brown Anxiety Research Project.

Table 5. Prevalence (%) of Comorbid Personality Disorders at the Time of Intake in HARP Study Subjects With Social Anxiety Disorder, Panic Disorder With and Without Agoraphobia, or Generalized Anxiety Disorder[a,b]

Type of Personality Disorder	Social Anxiety Disorder (N = 141)	Panic Disorder With Agoraphobia (N = 313)	Panic Disorder Without Agoraphobia (N = 73)	Generalized Anxiety Disorder (N = 155)
Any personality disorder	44	20	22	35
Avoidant	36	12	14	20
Borderline	8	4	3	7
Dependent	6	5	3	10
Histrionic	2	2	3	7
Obsessive-compulsive	7	5	6	9
Passive-aggressive	4	4	3	5

[a]Data from Dyck et al.[1]
[b]This table includes only personality disorders with a prevalence of 3% or higher.
Abbreviation: HARP = Harvard/Brown Anxiety Research Project.

Figure 4. Cumulative Relapse Rate in HARP Study Subjects With Anxiety Disorders or Major Depressive Disorder[a]



[a]M. B. Keller, M.D., unpublished data, 2004.
Abbreviations: GAD=generalized anxiety disorder, HARP = Harvard/Brown Anxiety Research Project, MDD = major depressive disorder, PD = panic disorder without agoraphobia, PDA = panic disorder with agoraphobia, SAD = social anxiety disorder.

RELAPSE AND RECURRENCE

A *relapse* or *recurrence* of SAD has been defined as symptoms meeting Research Diagnostic Criteria[6] or DSM-III-R criteria for SAD following an 8-week recovery period. In the HARP study, the cumulative relapse rate over a 10-year period (Figure 4) was lower in subjects with SAD (34%) than in subjects with GAD (38%), panic disorder without agoraphobia (54%), panic disorder with agoraphobia (55%), and major depressive disorder (82%). The time to a second relapse was shorter than the time to a first relapse (i.e., the duration of the interval of wellness decreased over time) (M.B.K., unpublished data, 2004).

TREATMENT

In all HARP study subjects, the use of nonpharmacologic treatments for which empiric efficacy data are available (e.g., cognitive and behavioral methods) was low early in the course of the illness (Table 6). Use of these treatment methods decreased over an 8-year follow-up period, possibly in part due to a lack of efficacy. Supportive and psychodynamic treatment methods were used to a greater extent than cognitive and behavioral methods and relaxation/meditation techniques early in the course of illness. The use of supportive and psychodynamic methods declined over the same 8-year period, but the reduction was not as large as the reduction in cognitive and behavioral methods (unpublished HARP data, 1991–1999; Goisman RG, Bruce SE, Vasile R, et al.).

Treatment was used to a lesser extent for SAD than for the other 3 anxiety disorders. The percentage of subjects with SAD who received any psychotropic drug therapy

Table 6. Trends in Types of Nonpharmacologic Treatment Received by All HARP Study Subjects[a]

	% of Subjects Receiving Therapy							
Type of Treatment	6-Month Follow-Up (N = 662)	2-Year Follow-Up (N = 607)	3-Year Follow-Up (N = 497)	4-Year Follow-Up (N = 285)	5-Year Follow-Up (N = 358)	6-Year Follow-Up (N = 449)	7-Year Follow-Up (N = 455)	8-Year Follow-Up (N = 415)
Relaxation/meditation	26	28	18	19	19	14	11	9
Any behavioral methods	33	30	26	22	22	18	16	11
Any cognitive methods	37	39	30	28	28	22	17	14
Any supportive methods	76	70	65	59	55	55	46	42
Any psychodynamic methods	57	55	47	41	42	41	31	22

[a]M.B. Keller, 8-year HARP data, 2003.
Abbreviation: HARP = Harvard/Brown Anxiety Research Project.

Table 7. Trends in Psychotropic Drug Use During SAD Episodes in the HARP Study[a]

	% of Subjects Receiving Therapy					
Pharmacotherapy	1989–1991 Time of Intake (N = 168)	1991–1993 2-Year Follow-Up (N = 174)	1991–1995 4-Year Follow-Up (N = 158)	1995–1997 6-Year Follow-Up (N = 146)	1997–1999 8-Year Follow-Up (N = 128)	1999–2001 10-Year Follow-Up (N = 100)
Any psychotropic therapy	75	68	69	70	77	73
No psychotropic therapy	25	32	31	30	28	27
SSRIs	18	16	22	29	34	33
Benzodiazepines	56	50	52	50	51	51
Tricyclic antidepressants	20	19	2	16	11	11
Heterocyclic agents[b]	5	11	9	12	21	23
Nonbenzodiazepine anxiolytic agents	5	5	2	2	3	2

[a]Unpublished HARP data, 1991–1999, Goisman RG, Bruce SE, Vasile R, et al.
[b]Heterocyclic agents include bupropion and venlafaxine.
Abbreviations: HARP = Harvard/Brown Anxiety Research Project; SAD = social anxiety disorder; SSRIs = selective serotonin reuptake inhibitors.

did not change substantially over a 10-year follow-up period (Table 7). About 75% of subjects with SAD received psychotropic drug therapy during the most recent time frame for which data are available (1999–2001) (Goisman RG, Bruce SE, Vasile R, et al., unpublished HARP data, 1991–1999).

The use of selective serotonin reuptake inhibitors (SSRIs) increased nearly 2-fold in subjects with SAD over the 10-year period, although use remained low (only 1 in 3 subjects) during 1999–2001.[7] A greater increase in SSRI use might have been observed if the selective serotonin-norepinephrine reuptake inhibitor venlafaxine had been grouped with the SSRIs instead of with the heterocyclic agents. Benzodiazepine use did not decrease over the 10-year period, with approximately half the patients with SAD taking a benzodiazepine, a finding that is surprising since benzodiazepines are now considered second-line therapies, although at least 2 studies show a large effect.[8,9]

IMPLICATIONS

Evaluation of patients with SAD for comorbid anxiety, depressive, and personality disorders is warranted because of the high rates of comorbidity with these disorders in patients with SAD observed in HARP study subjects. The chronic nature of SAD and low recovery rates over the long term in this study suggest that long-term treatment may be required to effect a recovery. Research in patients with chronic or recurrent SAD is needed to evaluate the impact of long-term treatment on recovery rates.

SUMMARY

SAD is a common anxiety disorder with an early onset and a deleterious effect on social functioning that is greater than that of depressive symptoms and chronic medical conditions. A high rate of comorbid anxiety, depressive, and personality disorders is associated with SAD. SAD is a chronic disorder with a lower long-term rate of recovery than other anxiety disorders, although SAD has a lower relapse rate once recovery is achieved. Treatment is underutilized in patients with SAD. It may be needed on a long-term basis to produce a recovery.

Drug names: bupropion (Wellbutrin and others), venlafaxine (Effexor and others).

Disclosure of off-label usage: Paroxetine, sertraline, and venlafaxine are approved by the U.S. Food and Drug Administrative (FDA) for the treatment of social anxiety disorder. The author has determined that, to the best of his knowledge, bupropion is not approved by the FDA for the treatment of social anxiety disorder.

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