Comorbidity of Fibromyalgia and Psychiatric Disorders

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Objective: To assess the co-occurrence of fibromyalgia with psychiatric disorders in participants of a fibromyalgia family study.

Method: Patients (probands) with fibromyalgia, control probands with rheumatoid arthritis, and first-degree relatives of both groups completed a structured clinical interview and tender point examination. The co-occurrence odds ratio (OR) (the odds of a lifetime comorbid DSM-IV disorder in an individual with fibromyalgia divided by the odds of a lifetime comorbid disorder in an individual without fibromyalgia, adjusted for age and sex) was calculated; observations were weighted by the inverse probability of selection, based on the fibromyalgia status of the proband; and standard errors were adjusted for the correlation of observations within families. The study was conducted from September 1999 to April 2002.

Results: We evaluated 78 fibromyalgia probands and 146 of their relatives, and 40 rheumatoid arthritis probands and 72 of their relatives. Among the relatives of both proband groups, we identified 30 cases of fibromyalgia, bringing the total number of individuals with fibromyalgia to 108, compared with 228 without fibromyalgia. The co-occurrence ORs for specific disorders in individuals with versus those without fibromyalgia were as follows: bipolar disorder: 153 (95% CI = 26 to 902, $p < .001$); major depressive disorder: 2.7 (95% CI = 1.2 to 6.0, $p = .013$); any anxiety disorder: 6.7 (95% CI = 2.3 to 20, $p < .001$); any eating disorder: 2.4 (95% CI = 0.36 to 17, $p = .36$); and any substance use disorder: 3.3 (95% CI = 1.1 to 10, $p = .040$).

Conclusions: There is substantial lifetime psychiatric comorbidity in individuals with fibromyalgia. These results have important clinical and theoretical implications, including the possibility that fibromyalgia might share underlying pathophysiologic links with some psychiatric disorders.

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Fibromyalgia is a chronic musculoskeletal pain disorder of unknown etiology that is defined by the American College of Rheumatology as widespread pain of at least 3 months' duration in combination with tenderness at 11 or more of 18 specific tender point sites on the body.[1] Fibromyalgia occurs in approximately 2% of the general population in the United States and is more common in women than in men, affecting 3.4% of women compared with 0.5% of men.[2]

Results of previous studies of comorbidity suggest that, in both community and clinic groups, fibromyalgia is strongly associated with multiple somatic complaints and depressive and anxiety symptoms as well as a personal and family history of depression and accompanying antidepressant treatment.[3,4] Patients with fibromyalgia have also been reported to have significantly higher lifetime

rates of mood and anxiety disorders and more somatic symptoms than patients with rheumatoid arthritis, another disorder characterized by chronic pain.[5–7]

Our group recently completed a controlled family study of fibromyalgia in which we found that fibromyalgia aggregates in families.[8] We also found that fibromyalgia coaggregates in families with major mood disorders[8] as well as with mood disorders, anxiety disorders, eating disorders, irritable bowel disorder, and migraine taken collectively.[9] These results, and the previous findings that mood and anxiety disorders are frequently comorbid with fibromyalgia, suggest that fibromyalgia may share a common physiologic abnormality with some psychiatric and medical disorders.

To evaluate further the relationship between fibromyalgia and psychiatric disorders, we used diagnostic data collected from the family study participants to assess the co-occurrence of fibromyalgia with psychiatric disorders in individuals, specifically the within-person association of disorders, rather than the familial association of disorders. To our knowledge, this is the largest controlled study of lifetime psychiatric comorbidity in fibromyalgia. Our hypothesis was that individuals with fibromyalgia would be significantly more likely than those without fibromyalgia to have comorbid mood and anxiety disorders.

METHOD

Patient Selection and Assessment

Full details of patient (proband) selection and assessment are presented in Arnold et al.[8] Briefly, from September 1999 to April 2002, we recruited probands with fibromyalgia and probands with rheumatoid arthritis without a lifetime diagnosis of fibromyalgia from consecutive referrals to 2 community rheumatology outpatient practices. A comparison group of probands with rheumatoid arthritis was chosen as a non-fibromyalgia proband control group because these probands were also seeking treatment at the same centers for a chronic, painful musculoskeletal condition. The use of probands with rheumatoid arthritis as a control group reduces the possibility of ascertainment bias due to the effects of seeking treatment for a chronic painful condition.

In an attempt to optimize the design of the family study from which data used here were obtained, probands in both groups were required to be 40 to 55 years old (to obtain a sample of relatives with a broad mixture of children, siblings, and parents that was similar across proband groups) and to have at least 1 first-degree relative available for interview and examination. Probands with fibromyalgia were diagnosed with a comprehensive clinical evaluation using the American College of Rheumatology criteria[1]; they were excluded if they had other rheumatologic disorders. Probands with rheumatoid arthritis were diagnosed using the American College of Rheumatology 1987 revised criteria[10] and were excluded if they had fibromyalgia or other rheumatologic disorders. First-degree relatives were eligible for the study if they were at least 18 years old (since younger subjects would have spent little time in the period of risk for fibromyalgia and the other conditions under study) and had no condition that would prevent them from being interviewed (e.g., dementia). All probands and interviewed relatives provided written informed consent for the study after all study procedures were explained and before any study procedures were performed. The University of Cincinnati Institutional Review Board approved the study protocol.

Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) lifetime diagnoses[11] were determined using the Structured Clinical Interview for DSM-IV Axis I Disorders–Patient Edition (SCID-I/P),[12] together with an additional module for fibromyalgia in SCID format.[13] All participants also underwent a tender point evaluation to assess for fibromyalgia using the American College of Rheumatology criteria.[1] One investigator (L.M.A.) conducted the interviews of the fibromyalgia and rheumatoid arthritis probands and completed the tender point examinations for all participants. Another investigator (M.B.A.), who was blinded to the proband diagnosis, conducted the interviews of the relatives.

Statistical Analysis

To test the hypothesis that individuals with fibromyalgia are significantly more likely than those without fibromyalgia to have comorbid mood and anxiety disorders, we used the co-occurrence odds ratio (OR), which is the odds of a lifetime comorbid disorder in an individual with fibromyalgia divided by the odds of a lifetime comorbid disorder in an individual without fibromyalgia. We calculated 3 ORs: for probands only, for relatives only, and for probands and relatives combined. In the ORs for relatives and for the combined group, we adjusted for age and sex; in the OR for probands, we adjusted only for age because there were no male probands with fibromyalgia.

To correct for the effects of sampling induced by selecting families of fibromyalgia probands at a higher frequency than families of non-fibromyalgia probands (rheumatoid arthritis group), we weighted observations by the inverse probability of selection, based on the fibromyalgia status (present or absent) of the proband in the family; relatives are thereby weighted to represent a random sample of the source population that gave rise to the fibromyalgia probands. We used a method for obtaining prevalence estimates for disorders using the relatives in case-control sampled probands (K.N.J.; N. M. Laird, Ph.D.; J.I.H., unpublished data; available from authors by request) to estimate the prevalence of fibromyalgia. The formula for calculating the prevalence of fibro-

Table 1. Lifetime Prevalence of Psychiatric Disorders in Patients and Relatives With and Without Fibromyalgia

Disorder	Patient Probands		Relatives		Probands and Relatives Combined	
	Fibromyalgia (N = 78), N (%)	Rheumatoid Arthritis (No Fibromyalgia) (N = 40), N (%)	Fibromyalgia (N = 30), N (%)	No Fibromyalgia (N = 188), N (%)	Fibromyalgia (N = 108), N (%)	No Fibromyalgia (N = 228), N (%)
Mood disorders						
Bipolar disorder	10 (12.8)	0	2 (6.7)	3 (1.6)	12 (11.1)	3 (1.3)
Major depressive disorder	48 (61.5)	11 (27.5)	19 (63.3)	64 (34.0)	67 (62.0)	75 (32.9)
Major mood disorder	58 (74.4)	11 (27.5)	21 (70.0)	67 (35.6)	79 (73.1)	78 (34.2)
Dysthymic disorder[a]	1 (1.3)	0	1 (3.3)	4 (2.1)	2 (1.9)	4 (1.8)
Anxiety disorders						
Generalized anxiety disorder[a]	4 (5.1)	3 (7.5)	1 (3.3)	6 (3.2)	5 (4.6)	9 (3.9)
Obsessive-compulsive disorder	5 (6.4)	0	2 (6.7)	4 (2.1)	7 (6.5)	4 (1.8)
Panic disorder[b]	22 (28.2)	3 (7.5)	9 (30.0)	12 (6.4)	31 (28.7)	15 (6.6)
Posttraumatic stress disorder	18 (23.1)	2 (5.0)	5 (16.7)	8 (4.3)	23 (21.3)	10 (4.4)
Social phobia	16 (20.5)	2 (5.0)	5 (16.7)	5 (2.7)	21 (19.4)	7 (3.1)
Specific phobia	17 (21.8)	5 (12.5)	0	3 (1.6)	17 (15.7)	8 (3.5)
Agoraphobia without panic disorder	1 (1.3)	0	0	2 (1.1)	1 (0.9)	2 (0.9)
Any anxiety disorder	47 (60.3)	10 (25.0)	13 (43.3)	30 (16.0)	60 (55.6)	40 (17.5)
Eating disorders						
Anorexia nervosa	3 (3.8)	0	1 (3.3)	2 (1.1)	4 (3.7)	2 (0.9)
Binge-eating disorder	3 (3.8)	1 (2.5)	3 (10.0)	2 (1.1)	6 (5.6)	3 (1.3)
Bulimia nervosa	2 (2.6)	0	2 (6.7)	1 (0.5)	4 (3.7)	1 (0.4)
Any eating disorder	7 (9.0)	1 (2.5)	5 (16.7)	5 (2.7)	12 (11.1)	6 (2.6)
Substance use disorders						
Alcohol abuse/dependence	17 (21.8)	4 (10.0)	4 (13.3)	35 (18.6)	21 (19.4)	39 (17.1)
Drug abuse/dependence	12 (15.4)	1 (2.5)	3 (10.0)	18 (9.6)	15 (13.9)	19 (8.3)
Any substance use disorder	20 (25.6)	5 (12.5)	6 (20.0)	39 (20.7)	26 (24.1)	44 (19.3)
Somatoform disorders						
Hypochondriasis	1 (1.3)	0	0	0	1 (0.9)	0
Somatization disorder	1 (1.3)	0	1 (3.3)	0	2 (1.9)	0
Psychotic disorders						
Schizophrenia	1 (1.3)	0	0	0	1 (0.9)	0

[a]Current diagnosis only.
[b]With or without agoraphobia.

myalgia is $p_u/(1 - p_a + p_u)$, where p_a is the proportion of relatives of fibromyalgia probands with fibromyalgia and p_u is the proportion of relatives of non-fibromyalgia (rheumatoid arthritis) probands with fibromyalgia. This prevalence estimation method relies on the assumption of single ascertainment of families and also requires that the probability of proband selection be independent of the characteristics of his or her relatives (K.N.J.; N. M. Laird, Ph.D.; J.I.H., unpublished data). Because observations within families are correlated, we used generalized estimating equations to estimate standard errors.[14] We did not adjust standard errors for the uncertainty surrounding the estimation of weights because, in general, not doing so overestimates the true standard errors.[15]

Because many of the measures were correlated, it was difficult to calculate an appropriate correction for the effects of multiple comparisons. Therefore, the results are presented without correction, with the α set at .05, 2-tailed. Accordingly, the reader should bear in mind that some findings, especially those of marginal significance ($.01 < p < .05$), may represent chance associations. We used Stata 9.0 software (StataCorp, College Station, Tex.) for analyses.

RESULTS

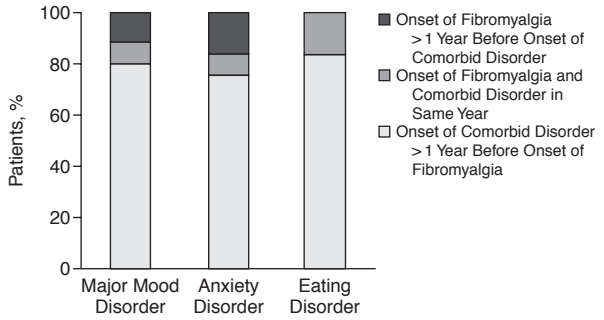
We evaluated 78 probands with fibromyalgia and 146 of their first-degree relatives, and 40 probands with rheumatoid arthritis and 72 of their first-degree relatives. There were 30 cases of fibromyalgia among the 218 total relatives of both proband groups (27 relatives of fibromyalgia probands and 3 relatives of rheumatoid arthritis probands), bringing the total number of fibromyalgia cases to 108, compared with 228 without fibromyalgia. The mean (SD) age of the 108 individuals with fibromyalgia was 47.9 (8.5) years; 105 (97%) were women, and 101 (94%) were white. The 228 individuals without fibromyalgia had a mean (SD) age of 53.1 (15.0); 83 (36%) were women, and 211 (93%) were white. The lifetime prevalence of psychiatric disorders in the proband groups, in relatives with and without fibromyalgia, and in the combined group of probands and relatives with and without fibromyalgia is shown in Table 1. There were no significant differences in the lifetime prevalence of psychiatric disorders between the 118 probands and the 218 total relatives, except for specific phobia, which was significantly more common in the probands than relatives (22/118 [18.6%] vs. 3/218 [1.4%], respectively; $p < .001$, by Fisher exact test, 2-tailed).

Table 2. Co-Occurrence of Fibromyalgia With Psychiatric Disorders[a]

	Co-Occurrence Odds Ratio (OR)								
	Patient Probands[b]			Relatives[c]			Probands and Relatives Combined[c]		
Disorder	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
Mood disorders									
Bipolar disorder	∞[d]	1.5 to ∞	.016	103	9.8 to 1083	< .001	153	26 to 902	< .001
Major depressive disorder	4.3	1.8 to 10	< .001	2.6	0.44 to 16	.29	2.7	1.2 to 6.0	.013
Major mood disorder	8.4	3.4 to 21	< .001	9.0	2.9 to 27	< .001	6.2	2.9 to 14	< .001
Dysthymic disorder	…			0.28	0.02 to 4.1	.35	0.48	0.07 to 3.5	.47
Anxiety disorders									
Generalized anxiety disorder	0.75	0.16 to 3.5	.71	2.5	0.31 to 27	.51	0.87	0.21 to 3.7	.86
Obsessive-compulsive disorder	∞[d]	0.69 to ∞	.17	2.9	0.31 to 27	.35	14	2.8 to 72	.001
Panic disorder	4.7	1.2 to 18	.024	3.7	0.40 to 33	.25	5.0	1.9 to 13	.001
Posttraumatic stress disorder	5.7	1.2 to 26	.025	30	4.0 to 226	< .001	12	2.9 to 51	< .001
Social phobia	4.8	1.03 to 22	.046	11	0.99 to 114	.051	8.9	2.2 to 36	.002
Specific phobia	1.7	0.56 to 5.0	.35	…			2.0	0.73 to 5.5	.18
Agoraphobia without panic disorder	…			…			4.0	0.37 to 45	.25
Any anxiety disorder	4.7	2.0 to 11	< .001	6.8	1.0 to 46	.48	6.7	2.3 to 20	< .001
Eating disorders									
Anorexia nervosa	…		.55	3.5	0.17 to 72	.42	13	2.0 to 82	.007
Binge-eating disorder	1.4	0.20 to 10	.73	1.1	0.07 to 19	.94	1.2	0.14 to 10	.86
Bulimia nervosa	…		.55	120	7.7 to 1863	< .001	74	4.7 to 1176	.002
Any eating disorder	4.2	0.52 to 31	.16	1.8	0.14 to 23	.66	2.4	0.36 to 17	.36
Substance use disorders									
Alcohol abuse/dependence	2.1	0.62 to 6.9	.23	1.2	0.27 to 5.2	.83	2.0	0.72 to 5.5	.18
Drug abuse/dependence	5.6	0.68 to 46	.11	3.1	0.25 to 40	.38	2.4	0.55 to 11	.24
Any substance use disorder	2.6	0.65 to 6.0	.23	3.6	0.59 to 22	.17	3.3	1.1 to 10	.040

[a]Somatoform disorders and psychotic disorders had insufficient data to compute odds ratio (fewer than 5 subjects with disorder).
[b]Except where noted otherwise, adjusted for age.
[c]Except where noted otherwise, adjusted for age and sex; observations weighted by inverse probability of selection, based on status of proband in family; standard errors adjusted for correlation of observations within families.
[d]Unadjusted odds ratio.
Abbreviation: CI = confidence interval.
Symbols: ∞ = infinity, … = insufficient data to compute odds ratio.

Figure 1. Temporal Pattern of Comorbidity of Fibromyalgia and Psychiatric Disorders



Compared with the combined group of probands and relatives without fibromyalgia, those with fibromyalgia were significantly more likely to have comorbid bipolar disorder, major depressive disorder, major mood disorder (major depressive disorder or bipolar disorder), panic disorder, posttraumatic stress disorder, social phobia, obsessive-compulsive disorder, any anxiety disorder, anorexia nervosa, bulimia nervosa, and any substance use disorder. There were no significant differences between relatives and probands in the degree of the comorbidity of fibromyalgia and other disorders. The co-occurrence ORs for each of the disorders in the probands, relatives, and the combined group are presented in Table 2. Among individuals with fibromyalgia and a co-occurring lifetime mood, anxiety, or eating disorder, the onset of the co-occurring disorder was usually greater than 1 year before the onset of fibromyalgia (Figure 1).

DISCUSSION

We found a significant association of fibromyalgia with mood disorders, anxiety disorders, eating disorders, and substance use disorders.

Mood Disorders

Individuals with fibromyalgia were significantly more likely than those without fibromyalgia to have comorbid major depressive disorder. This finding is consistent with some controlled,[5,7] uncontrolled,[16,17] and community-based[2,4] studies, but not all previous studies.[6,18] To provide a further comparison of previous studies with the results of the present study, we performed a meta-analysis of the 5 controlled studies that used structured diagnostic

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interviews[5–7,18,19] to assess major depressive disorder, using a random-effects model.[20] The meta-analytic odds ratios showed a significant degree of co-occurrence with major depressive disorder: OR (95% CI) of 3.6 (1.1 to 11), p = .031, which is similar to the OR obtained in the present study.

In addition to the co-occurrence of fibromyalgia and major depressive disorder, we also found that individuals with fibromyalgia were significantly more likely to have comorbid bipolar disorder than those without fibromyalgia. The co-occurrence of bipolar disorder in fibromyalgia patients has received little attention in previous studies. Only 1 previous study found comorbid bipolar disorder in 2 (6%) of 33 women with fibromyalgia.[16] The presence of comorbid bipolar disorder has important clinical implications, because antidepressants that are often used to treat fibromyalgia[21–23] may precipitate hypomanic, manic, or mixed episodes in predisposed individuals who have existing or latent bipolar disorder.[24]

Anxiety Disorders

We also found that individuals with fibromyalgia were significantly more likely than those without fibromyalgia to have comorbid anxiety disorders, including panic disorder, posttraumatic stress disorder, social phobia, and obsessive-compulsive disorder. These results are again consistent with other controlled,[5,7,19] uncontrolled,[16,17] and community-based[2,4] studies. We conducted a meta-analysis examining the co-occurrence of fibromyalgia with panic disorder and obsessive-compulsive disorder, again using the 5 studies cited above from our meta-analysis of fibromyalgia and major depressive disorder. We used a Mantel-Haentzel procedure to combine odds ratios in these cases because the estimates were too imprecise (due to small sample size) to use a random-effects model. The meta-analytic ORs (95% CI) showed a significant degree of co-occurrence of fibromyalgia with panic disorder (9.0 [3.5 to 23], p < .001) and obsessive-compulsive disorder (4.8 [1.0 to 23], p = .035). These results are also consistent with the ORs obtained in the present study.

The significant co-occurrence of fibromyalgia and posttraumatic stress disorder is consistent with prior studies that demonstrated high rates of posttraumatic stress disorder symptoms in patients with fibromyalgia,[25,26] a significant association between fibromyalgia and a lifetime diagnosis of posttraumatic stress disorder,[27] and marked comorbidity between posttraumatic stress disorder and fibromyalgia symptoms in a community-based study.[28] However, previous studies provide insufficient data to permit a meta-analysis of the type performed above. Even fewer studies have examined the relationship between fibromyalgia and social phobia, and more study of this disorder in patients with fibromyalgia is needed.

Eating Disorders

We also found a significant co-occurrence of anorexia nervosa and bulimia nervosa with fibromyalgia. This type of co-occurrence has not been previously reported, possibly because eating disorders are less common, and previous studies have had insufficient power to detect this association.

Substance Use Disorders

We found a significant co-occurrence between fibromyalgia and any substance use disorder, but this finding was only marginally significant (p = .040), and the co-occurrence with either alcohol use disorders or drug use disorders individually failed to reach significance. Previous controlled studies of the co-occurrence of fibromyalgia with dependence or abuse of alcohol[5,15] or drugs[5] have failed to find a significant co-occurrence, but they have had little power to detect co-occurrence. Of note is that in this sample we found no evidence that fibromyalgia coaggregated with substance use disorders in families.[9] On balance, the importance of a relationship, if any, between fibromyalgia and substance use disorders is unclear.

Overall Implications

Our findings have both practical and theoretical implications. On a practical level, given the frequent comorbidity of fibromyalgia with psychiatric disorders, clinicians should be alerted to inquire about these conditions when evaluating and treating patients with fibromyalgia. The overall outcome of treatment in such patients will be determined not only by the improvement of fibromyalgia itself, but also by the response of associated conditions.

On a theoretical level, our findings augment the growing evidence that fibromyalgia may be part of a larger group of disorders that may share common etiologic features. As we have proposed elsewhere, the findings lend support to the hypothesis that there are shared risk factors for fibromyalgia and mood and anxiety disorders,[8,9] as well as to affective spectrum disorder.[9] Evidence from 2 recent family studies of fibromyalgia suggests that fibromyalgia and mood disorders share common (and, possibly genetic) determinants.[8,29,30] For example, abnormalities in central monoaminergic neurotransmission might be involved in both mood and anxiety disorders and fibromyalgia.[8] In addition, recent neuroimaging studies point to the possibility that similar areas of the brain, such as the anterior cingulated cortex, might be involved in both the regulation of pain and emotional dysregulation of some anxiety disorders.[27] The observation in the present study that comorbid psychiatric disorders preceded the onset of fibromyalgia in most cases suggests that the psychiatric disorder does not usually develop simply as a consequence of having

fibromyalgia. The previously reported family study findings of coaggregation of major mood disorder and fibromyalgia[8] are also inconsistent with the hypothesis that fibromyalgia results from psychiatric disorders. Rather, the results of the present study and the family study are more consistent with the hypothesis of shared vulnerability for these psychiatric disorders and fibromyalgia.

More broadly, fibromyalgia is not only comorbid with psychiatric disorders, but with a number of other medical disorders—several of which also share similar patterns of psychiatric comorbidity. These include chronic fatigue syndrome, irritable bowel syndrome, multiple chemical sensitivity, interstitial cystitis, and others.[9,16,31–35] As we have reported previously,[9] the patient probands with fibromyalgia in this study had an elevated lifetime prevalence of chronic fatigue syndrome, irritable bowel syndrome, and migraine, as compared with the probands with rheumatoid arthritis; we did not assess other potentially related medical disorders. As we have discussed elsewhere,[31] similar sets of overlapping conditions have been referred to by various names, including "affective spectrum disorder,"[16,31,36] "dysfunctional spectrum syndrome,"[37] "neurosomatic disorders,"[38] and "functional somatic syndromes."[39] Family studies[9,32,40,41] suggest that common familial, and likely common genetic, factors underlie the predisposition to this set of medical and psychiatric disorders.

Several limitations of this study should be considered. First, there is the possibility of ascertainment bias for either the patient probands or the relatives. With regard to the probands, the results could be biased if the differential between patients with fibromyalgia and a random population sample of individuals with fibromyalgia in the population with respect to co-occurrence (the "co-occurrence differential") was greater or lesser than the co-occurrence differential between patients with rheumatoid arthritis and a random population sample of individuals without fibromyalgia in the population. It is likely that both patient groups would display a slightly higher prevalence of comorbid psychiatric conditions. One study[42] found a higher prevalence of psychiatric disorders in patients with fibromyalgia compared with individuals from the community with fibromyalgia who had not sought treatment. It should be noted, however, that the association of psychopathology with fibromyalgia is unlikely to be accounted for solely by the effect of ascertainment bias, because other community-based studies have found an association between psychiatric disorders and fibromyalgia[2,43] or chronic widespread pain.[4,44] Studies of individuals with rheumatoid arthritis have reported a slight excess of psychiatric comorbidity compared with the general population, which is similar in magnitude to that found in association with other chronic medical conditions.[43,45–47] In light of these considerations, it is likely that the co-occurrence differential would be similar in both patient groups. This impression is supported by the finding that the co-occurrence ORs in the relatives, who were not care-seeking, were nearly identical to those in the patients—a finding that also justifies combining the 2 groups for analysis.

With regard to the relatives, as we have discussed, ascertainment bias is much less likely. The weighting used for observations from relatives would be expected to produce a sample representative of the source population that gave rise to the patients with fibromyalgia. However, if the patient probands with fibromyalgia and rheumatoid arthritis were indeed more likely to have co-occurring psychiatric disorders than individuals with and without fibromyalgia, respectively, in the general population, then the sample of relatives would be biased somewhat toward having a higher prevalence of these conditions due to the effect of familial factors for these disorders. This bias, in turn, could influence co-occurrence ORs in the relatives. In the setting of approximately equal bias toward comorbidity in both patient groups, the effect would be to bias the ORs toward the null. There is also the possibility of ascertainment bias in findings from the relatives if the weighting procedure does not accurately yield the inverse of the true selection probabilities. However, substantial bias from this source is unlikely, in that the results are very similar even if no weighting is used.

Second, the source population that gave rise to the families may not be representative of the larger general population, thus potentially reducing generalizability. It should be considered that almost all of the participants were white, so the results may not generalize to populations with different racial and ethnic characteristics. Third, the interviewers were not blinded to the diagnosis of fibromyalgia in the participants. Thus, there is the possibility of observer bias if investigators were more likely or less likely to make diagnoses in individuals with fibromyalgia compared with individuals without fibromyalgia. However, while some observer bias may have been present, it seems unlikely to have greatly influenced the results. Fourth, all but 3 of the subjects with fibromyalgia were women. Therefore, it is possible the results would not generalize to men with fibromyalgia. Fifth, even though this is the largest study of the comorbidity of fibromyalgia and psychiatric disorders performed thus far, it is still not large enough to explore adequately many issues of importance.

In summary, we found that individuals with fibromyalgia were significantly more likely than those without fibromyalgia to have lifetime comorbid mood, anxiety, and eating disorders. These findings support the possibility of shared etiologic factors between fibromyalgia and these psychiatric disorders. Patients with fibromyalgia should be routinely evaluated for the presence of comorbid psychiatric disorders.

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