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Factor analysis of symptoms among subjects with unexplained chronic fatigue
What can we learn about chronic fatigue syndrome?

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Abstract

Objective: Chronic fatigue syndrome (CFS) case definitions agree that fatigue must be unexplained, debilitating and present for at least 6 months, but they differ over accompanying symptoms. Our objective was to compare the 1994 CFS case-defining symptoms with those identified by factor analysis. **Methods:** We surveyed the Wichita population and measured the occurrence of 21 symptoms in 1391 chronically fatigued subjects who did not report fatigue-associated medical or psychiatric conditions. We used factor analyses to identify symptom dimensions of fatigue and cluster analysis to assign subjects to subgroups. **Results:** Forty-three subjects had CFS. We confirmed three factors: musculoskeletal, infection and cognition–mood–sleep, essentially defined by CFS symptoms. Although factor scores were higher among CFS subjects, CFS and non-CFS distributions overlapped substantially. Three clusters also showed overlap between CFS and non-CFS subjects. **Conclusion:** CFS symptomatology is a multidimensional phenomenon overlapping with other unexplained fatiguing syndromes and this must be considered in CFS research.

Keywords: Case definition; CFS; Dichotomous factor analysis; Population-based survey; Symptoms; Unexplained fatigue

Introduction

For over a decade, the international scientific community has been challenged to accurately define chronic fatigue syndrome (CFS). All published CFS research case definitions [1–4] represent clinical consensus. The definitions agree that fatigue in such cases must be debilitating and present for 6 months or longer, and that CFS can be only diagnosed after ruling out other medical or psychiatric conditions that could cause fatigue. However, they differ with regard to accompanying symptoms, levels of functional impairment and exclusionary conditions [5]. For example, the current 1994 case definition [1] requires that fatigue should be accompanied by at least 4 of 8 symptoms, whereas the 1988 case definition [4] required 8 of 11 symptoms, and case definitions from 1990 [2] and 1991 [3] required no symptoms for CFS diagnosis.

The primary aim of this study was to address the controversy over CFS accompanying symptoms. For this purpose, we compared symptoms of the 1994 CFS case definition [1] with symptoms identified by use of factor analysis. Our second aim was to use this model to estimate the level of chronic unwellness associated with each symptom dimension (i.e., factor) of unexplained fatigue. To this end, we estimated factor scores for each subject. The objective was to perform cluster analysis of these measures to classify subjects with unexplained chronic fatigue into distinct subgroups. Finally, we explored how factor scores performed as stratifying variables when determining associations between risk factors and CFS.

Method

Participants

In 1997, the Centers for Disease Control and Prevention conducted a random-digit-dialing survey in Wichita, KS, to

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estimate the prevalence of CFS and other fatiguing illnesses [6]. The survey included screening and detailed telephone interviews, followed by a clinical evaluation of eligible subjects. In the screening interview, respondents were asked if they currently had severe fatigue, extreme tiredness or exhaustion lasting for ≥ 1 month. In the detailed interview, each fatigued subject and an equal number of randomly selected nonfatigued persons were queried concerning the presence of 21 other symptoms and a diagnosis of exclusionary medical and psychiatric illnesses potentially associated with fatigue (e.g., alcohol or drug dependency, anorexia nervosa or bulimia, cancer within 5 years, emphysema, chronic hepatitis or cirrhosis, heart conditions or stroke within the past 2 years, AIDS, lupus or Sjögren's syndrome, bipolar disorder, multiple sclerosis, rheumatoid arthritis, schizophrenia and organ transplantation). Fatigued persons were also asked about fatigue duration and severity. Subjects were eligible for a clinical evaluation if they have been fatigued for ≥ 6 months, their fatigue was not substantially alleviated by rest, they did not have any exclusionary conditions, and they reported at least four of the eight following CFS symptoms: impaired memory or concentration, sore throat, tender cervical or axillary lymph nodes, muscle pain, multijoint pain, new headaches, unrefreshing sleep and postexertion malaise [1]. A self-administered questionnaire, complete physical exam, laboratory tests and the Diagnostic Interview Schedule for DSM-IV [7] were conducted to determine if all CFS criteria [1] were satisfied (i.e., confirm the eligibility criteria for clinical evaluation and whether fatigue substantially affected personal, social, educational or work activities). Subjects satisfying all criteria were classified with CFS according to the 1994 case definition [1]. The Institutional Review Board of the Centers for Disease Control and Prevention approved the protocol of this study.

Because the current study was concerned about unexplained fatigue, subjects reporting any exclusionary medical or psychiatric conditions were dropped from the analyses.

Symptoms

During the detailed telephone interview, respondents were asked if any of 21 symptoms had been serious health problems during the previous 4 weeks. Those who reported having a symptom were further asked if its duration was <6 months or ≥ 6 months (chronic). Chronic symptoms were scored as 1, and symptoms absent or present for <6 months were scored as 0.

Fatiguing illness subgroups

Subjects were categorized into one of five subgroups: subjects who satisfied all CFS criteria [1] during a clinical evaluation (CFS), subjects with sufficient CFS criteria on basis of telephone information that could not be confirmed during a clinical evaluation (e.g., subjects who declined to be evaluated or did not meet CFS criteria during evaluation) (CFS-like), subjects with chronic fatigue of ≥ 6 months but insufficient CFS criteria on the basis of telephone information (CF), subjects with prolonged fatigue lasting 1 to <6 months and nonfatigued subjects.

Statistical analyses

We focused on subjects with unexplained chronic fatigue to compare symptoms defined by the 1994 case definition with those symptoms identified from a factor analysis model. Because symptoms were scored on a 0–1 basis, we used the dichotomous factor analysis model [8] to identify groups of the most correlated symptoms. A linear model could yield biased and inefficient estimates of factor loadings [8] or overestimate the number of factors [9]. We randomly split the overall sample in half for exploratory and confirmatory factor analyses. Exploratory factor analyses determined the number of factors underlying the symptom correlations and identified those symptoms most correlated with each factor (factor structure). Confirmatory factor analyses assessed the reproducibility of factor structures from the exploratory phase. We estimated tetrachoric correlations [8] and performed exploratory analyses with Promax oblique rotation [10] to estimate the correlation among the factors. Symptoms were initially screened to determine whether tetrachoric correlations were estimated with sufficient precision [8] (i.e., the number of subjects endorsing each pair of symptoms was ≥ 5). We estimated the number of factors in the exploratory phase from the scree plot [10] and used a robust weighted least-squares estimator [11] to estimate factor loadings. The number of factors was considered sufficient to explain symptom correlations if the root mean square error of approximation (RMSEA) was ≤ 0.06 [11,12]. Since in general, factor loadings are considered meaningful when they exceed .30 or .40 [10], we determined the stability of the factor structures by repeating the exploratory analyses and dropping symptoms with factor loadings of $<.35$. We used a confirmatory model [11] that specified the number of factors and the leading symptom (i.e., one with highest loading) in each factor to test the exploratory structure. The model was deemed to fit the data well if any of the following goodness-of-fit indices was satisfied: RMSEA of ≤ 0.06, Tucker–Lewis Index (TLI) of ≥ 0.95, Comparative Fit Index (CFI) of ≥ 0.95 or standardized root mean square residual (SRMR) of ≤ 0.08 [11–13]. Subjects from the exploratory and confirmatory samples were pooled, symptom data were fit to the final confirmatory model, and scores for each factor were estimated as nonlinear functions of the factor loadings and prevalence of symptoms [8]. Factor scores were considered as measures of chronic unwellness associated with each factor. Cluster analysis of factor scores, using Ward's minimum variance algorithm [14], was performed to assign subjects to distinct categories. We used Mplus software [11] to perform factor analyses and estimate factor scores, and SAS [15] was used for all other analyses.

Results

Description of the original sample

Of 7162 subjects who responded to the detailed telephone interview, 2182 (30.5%) reported a medical or psychiatric exclusionary condition either on the detailed interview ($n = 2004$) or clinical evaluation ($n = 178$). These subjects were dropped from all analyses. Among the 4980 (69.5%) subjects who did not report any exclusionary condition, 7 had information missing in one or more symptoms and 4973 (99.9%) provided answers to all symptom questions. Table 1 displays the demographic characteristics and prevalence of chronic symptoms for these subjects. There were 3007 (60.5%) subjects who did not report fatigue, 575 (11.6%) reporting prolonged fatigue of 1 to <6 months, 1085 (21.8%) with CF, 263 (5.3%) with CFS-like and 43 (0.8%) classified with CFS. Sex, age and race distributions varied by illness subgroups (all χ^2 tests, P values < .01). Among subjects with chronic fatigue, CFS persons were more likely to be female and older (≥40 years) than were CFS-like or CF persons. The prevalence of symptoms increased with fatigue duration. Of interest, unrefreshing sleep was one of the most prevalent symptoms in all groups. In addition, 1.7% of nonfatigued, 14.6% of prolonged fatigue and 21.8% of chronic fatigue subjects had at least four of the eight CFS case-defining symptoms.

All subsequent analyses consider only the 1391 subjects with unexplained chronic fatigue.

Dichotomous factor analyses

The exploratory factor analysis sample included 718 respondents. Tetrachoric correlations ranged from .013 (between diarrhea and forgetfulness) to .782 (between muscle pain and joint pain) with a median of .29. All tetrachoric correlations were estimated with sufficient precision and, therefore, all symptoms were considered in the analysis. From the scree plot (figure not shown), we estimated that one to five factors (first 10 eigenvalues = 7.32, 1.88, 1.52, 1.30, 1.14, 1.1, 0.9, 0.83, 0.71, 0.63) were necessary to explain the correlations among the symptoms. The one-factor model was not sufficient to explain the correlations among symptoms because the RMSEA was 0.08, and the five-factor solution yielded uninterpretable factor loadings. Table 2 displays the solutions for two-, three- and four-factor analyses (RMSEA ≤ 0.06). In the two-factor solution, the first factor included musculoskeletal, flu-like

Table 1
Demographic characteristics and prevalence of symptoms lasting ≥6 months by fatiguing illness subgroup

	Fatiguing illness subgroup[a]					
	NF ($N = 3007$)	PF ($N = 575$)	CF ($N = 1085$)	CFS-like ($N = 263$)	CFS ($N = 43$)	All subjects with chronic fatigue ($N = 1391$)
Female sex	55.6	68.7	71.8	76.8	86.1	73.2
Age ≥ 40	51.9	46.1	60.8	60.1	76.7	61.2
White race	85.7	80.7	87.2	86.3	93.0	87.2
Unrefreshing sleep	10.5	29.6	53.4	93.9	93.0	62.3
Problems getting to sleep or waking up early in the morning	17.4	38.4	54.7	83.3	81.4	61.0
Muscle aches or muscle pain	9.8	25.7	38.8	90.1	95.3	50.3
Joint pain	14.6	31.7	39.9	82.1	90.7	49.4
Sinus or nasal problems	21.9	32.5	44.1	57.4	69.8	47.4
Depression	4.9	27.1	40.9	57.8	62.8	44.8
Forgetfulness or memory problems	7.2	27.1	37.9	64.3	83.7	44.3
General weakness	2.0	17.4	36.3	68.4	76.7	43.6
Difficulty thinking or concentrating	4.9	21.6	35.5	70.0	76.7	43.3
Unusual fatigue following exertion	1.6	14.4	32.8	77.2	74.4	42.5
Eyes extremely sensitive to light	11.3	26.1	29.0	60.1	53.5	35.7
Severe headaches	6.7	24.2	25.8	62.4	55.8	33.6
Numbness or tingling	5.7	20.9	27.0	50.6	55.8	32.4
Shortness of breath	4.8	16.7	28.2	46.4	53.5	32.4
Stomach or abdominal pain	3.5	12.7	20.4	38.4	30.2	24.1
Diarrhea	1.5	5.6	12.4	29.7	11.6	15.7
Nausea	1.0	5.9	10.6	26.6	25.6	14.1
Tender lymph nodes	0.5	2.4	6.8	24.3	20.9	10.6
Chills	0.4	3.7	7.2	23.6	16.3	10.6
Sore throat	0.7	2.6	4.7	13.7	14.0	6.7
Fever	0.2	1.7	3.7	15.6	14.0	6.3
≥4 CFS symptoms	1.7	14.6	21.8	100.0	100.0	13.7

[a] NF, no fatigue; PF, prolonged fatigue of 1 to <6 months; CF, chronic fatigue with insufficient CFS criteria; CFS-like, chronic fatigue with sufficient CFS criteria that could not be confirmed during a clinical evaluation; CFS, chronic fatigue syndrome confirmed by a clinical evaluation.

and gastrointestinal symptoms, and the second factor included cognition, mood and sleep disturbance symptoms. In the three-factor structure, musculoskeletal symptoms were in the first factor, flu-like and gastrointestinal symptoms were in the second, and cognition, mood and sleep disturbances were in the third. The four-factor solution represented a further partition of the three-factor solution and included separate factors for flu-like and gastrointestinal symptoms. All solutions yielded moderately correlated factors (factor correlations range=.4–.65). We assessed the stability of the two-, three-, and four-factor solutions by dropping symptoms with loadings of <.35 in all factors and repeating the exploratory analyses. The two-factor structure remained unchanged, but both the three- and four-factor solutions yielded different factor structures (data not shown). Therefore, to maintain stable structures, it was necessary to keep shortness of breath in the three-factor solution and all symptoms in the four-factor solution before conducting the confirmatory analysis.

The confirmatory sample included 673 respondents. We tested the exploratory solutions by specifying the number of factors to be two, three or four and by specifying the leading symptom in each factor of each solution. For example, in the two-factor model, muscle pain was the leading symptom in the first factor and difficulty thinking or concentrating was the leading symptom in the second factor. The two- and three-factor solutions were fairly similar to those from the exploratory analyses (data not shown). At least one measure of goodness-of-fit for each model was satisfactory: RMSEA = 0.058 and 0.051; SRMR = 0.083 and 0.070; CFI = 0.91 and 0.93; TLI = 0.92 and 0.94, for the two- and three-factor models, respectively. The four-factor model could not be confirmed. Although the two- and three-factor models yielded reasonable goodness-of-fit measures when the overall sample (N = 1391) was considered, the three-factor solution provided a more interpretable factor structure (Table 3). Factor correlations estimated from the confirmatory models were smaller than those estimated from the exploratory model.

Clinical consensus versus factor analysis

The factor analysis models identified all 1994 CFS case-defining symptoms, except severe headaches, as elements of distinct symptom dimensions (i.e., factors) of unexplained chronic fatigue. For example, in the three-factor model, there were three CFS symptoms in the first factor (muscle pain, joint pain, unusual fatigue after exertion), two CFS symptoms in the second factor (sore throat, tender lymph nodes) and two CFS symptoms in the third factor (difficulty thinking and forgetfulness, which were considered as only one symptom in the case definition, and unrefreshing sleep).

Table 2
Factor loadings (× 100) for exploratory dichotomous two-, three- and four-factor analyses of 21 chronic symptoms among 718 subjects with unexplained chronic fatigue

	Factor analyses								
	Two factors[a]		Three factors[b]			Four factors[c]			
Symptoms	1	2	1	2	3	1	2	3	4
Muscle aches or pain	100	−24	102	2	−21	93	14	−14	−3
Joint pain	93	−26	90	2	−21	87	17	−13	−12
Numbness or tingling	40	20	51	−9	22	39	−15	15	29
General weakness	37	32	38	3	30	25	10	21	41
Unusual fatigue postexertion	45	16	48	1	15	36	−10	8	35
Sore throat	71	−4	−7	88	−9	5	79	−1	0
Tender lymph nodes	76	−6	5	86	−15	10	72	−11	16
Fever	68	8	−4	82	3	8	80	12	−7
Chills	60	9	20	52	3	23	47	6	8
Nausea	39	29	−5	58	21	−28	27	5	78
Diarrhea	52	−10	14	50	−17	6	33	−22	37
Stomach or abdominal pain	45	14	8	50	6	−10	21	−10	68
Difficulty thinking or concentrating	−27	104	−20	−4	101	−19	−1	93	11
Forgetfulness or memory problems	−27	93	−14	−13	92	−11	−8	86	3
Depression	−8	58	0	−7	57	2	−1	53	3
Problems getting to sleep or waking up early in the morning	14	53	5	15	50	10	27	51	−11
Unrefreshing sleep	24	51	16	15	48	21	28	50	−12
Eyes extremely sensitive to light	35	18	25	17	16	18	10	11	23
Severe headaches	28	24	5	32	19	0	25	15	20
Shortness of breath	27	21	32	−1	20	15	−24	8	54
Sinus or nasal problems	20	23	−12	42	18	−13	31	14	20

[a] RMSEA = 0.055; factor correlation between factor 1 and factor 2 (1,2)=.65.
[b] RMSEA = 0.046; factor correlations: (1,2)=.63; (1,3)=.59; and (2,3)=.56.
[c] RMSEA = 0.036; factor correlations: (1,2)=.45; (1,3)=.49; (2,3)=.40; (2,4)=.46; and (3,4)=.49.

Table 3
Factor loadings (× 100) for confirmatory dichotomous three-factor analysis of 21 chronic symptoms among all of 1391 subjects with unexplained chronic fatigue

	Factors		
Symptoms	1	2	3
Musculoskeletal			
Muscle aches or pain[a]	89	0	0
Joint pain[a]	88	− 11	− 4
Numbness or tingling	50	− 5	21
Unusual fatigue postexertion[a]	49	5	22
General weakness	40	6	35
Shortness of breath	31	8	23
Infection			
Sore throat[a]	0	72	0
Tender lymph nodes[a]	11	70	− 2
Nausea	− 8	61	19
Fever	19	57	15
Diarrhea	9	55	0
Stomach or abdominal pain	− 1	55	18
Chills	28	41	14
Sinus or nasal problems	0	34	17
Cognition–mood–sleep			
Difficulty thinking or concentrating[a]	0	0	90
Forgetfulness or memory problems[a]	6	− 7	78
Unrefreshing sleep[a]	39	− 4	49
Depression	5	− 3	50
Problems getting to sleep or waking up early in the morning	29	− 2	47

RMSEA = 0.051; SRMR = 0.061; CFI = 0.93; TLI = 0.94.
Factor correlations: (1,2)=.55; (1,3)=.27; (2,3)=.33.
[a] 1994 CFS case-defining symptoms.

In general, CFS symptoms were good indicators of each factor because they had high loadings in the specific factor and small loadings on the other factors.

Factor scores to measure chronic unwellness

We focused on the three-factor model to measure and compare levels of chronic unwellness across fatiguing illness subgroups. Reflecting their symptom composition, we labeled the factors musculoskeletal symptoms, infection symptoms and cognition–mood–sleep symptoms. Factor scores were approximately normally distributed and standardized to have mean 0 and variance 1 (Fig. 1). In each factor, highly positive scores indicated high levels of symptom grouping and highly negative values reflected no symptoms or very few chronic symptoms. Although CFS subjects had significantly higher scores than CF subjects (median = 0.76 vs. − 0.24, 0.36 vs. − 0.24, 0.70 vs. − 0.21 for musculoskeletal, infection and cognition–mood–sleep symptoms, respectively, Wilcoxon test, P value < .0001 for all comparisons), there was some overlap between score distributions. For example, 13.9% and 74.4%, 18.3% and 32.6%, and 17.8% and 58.2% of the CFS and CF scores, respectively, were above the 75th percentile of each factor score distribution among all subjects (musculoskeletal symptoms, 0.632; infection symptoms, 0.559; cognition–mood–symptoms, 0.629). Thus, musculoskeletal symptoms seem to discriminate CFS and CF subjects better than the other two factors. Finally, CFS subjects were not significantly different from CFS-like subjects.

Application of factor scores

We explored the possibility that cluster analysis of the three factor scores could be useful in assigning subjects to distinct subgroups. Three major clusters were identified (data not shown). The proportion of variance explained by the three clusters was 0.55. Table 4 displays summaries of

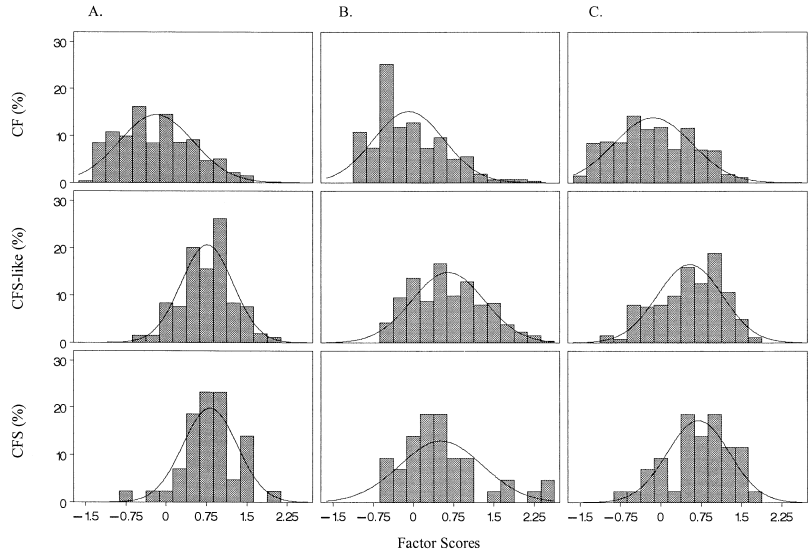

Fig. 1. Distribution of musculoskeletal (A), infection (B) and cognition–mood–sleep (C) symptom scores by fatiguing illness subgroup among subjects with unexplained chronic fatigue. Subgroups: CF, subjects with insufficient CFS criteria; CFS-like, subjects reporting sufficient CFS criteria that were not confirmed by a clinical evaluation; CFS, subjects clinically evaluated and classified with chronic fatigue syndrome.

the factor scores, total number of symptoms, duration of fatigue, self-reported energy on a scale of 1–100, sex and age for each cluster, as well as the distribution of fatiguing illness subgroups across clusters. A small subset of chronic fatigue subjects was assigned to the first cluster, and the remaining subjects were unevenly distributed across the second and third clusters. Therefore, agreement between clusters and fatigue subgroups was poor (kappa statistic=.0083). The third cluster included most of the CFS subjects and those who were most chronically unwell. The first cluster represented the healthiest subjects.

Factor scores were also used as stratifying variables to determine associations between risk factors and CFS. For example, the odds ratio (95% confidence interval) for the association between female sex and CFS (compared with chronic fatigue subjects) was 2.42 (1.01–5.80), with a *P* value of .047. However, the odds ratios and 95% confidence intervals for the associations between sex and CFS among subjects below and above the 75th percentile of the overall scores distribution of cognition–mood–sleep symptoms were 8.62 (1.14–65.36) and 1.04 (0.37–2.95), respectively. The different odds ratios (Breslow–Day test, *P* value=.042) between the categories indicated a significant interaction between unwellness levels and sex. In other words, the effect of female sex on CFS, when compared with CF, varied by unwellness levels. Using factor scores in their original continuous scale (instead of dichotomizing values above and below the 75th percentile) as a covariate in a logistic regression model yielded similar results (data not shown).

Table 4
Characteristics of the three clusters of subjects with unexplained chronic fatigue

	Clusters		
	1 (*n*=232)	2 (*n*=704)	3 (*n*=455)
Fatiguing illness subgroup[a]			
CF	232	624	229
CFS-like	0	71	192
CFS	0	9	34
Mean (S.D.) factor scores			
Musculoskeletal	−0.96 (0.26)	−0.13 (0.52)	0.75 (0.53)
Infection	−0.75 (0.27)	−0.16 (0.43)	0.82 (0.57)
Cognition–mood–sleep	−0.83 (0.36)	−0.13 (0.63)	0.66 (0.50)
Median (range) of total number of symptoms	2 (0–6)	5 (1–11)	11 (5–20)
Median (range) months of fatigue duration	16 (6–449.1)	24.5 (6–771.4)	38.9 (6–603.7)
Mean (S.D.) self-reported energy levels	58 (22)	54.3 (20.3)	46.2 (21.6)
% Female	65.5	72.7	77.8
Mean (S.D.) age, years	41.1 (12.8)	44.4 (12.4)	43.8 (11.3)

[a] CF, chronic fatigue with insufficient CFS criteria; CFS-like, chronic fatigue with sufficient CFS criteria that could not be confirmed during a clinical evaluation; CFS, chronic fatigue syndrome confirmed by a clinical evaluation.

Discussion

The first CFS case definition, which was published in 1988 [4], stated that CFS was "an operational concept designed for research purposes that physicians must recognize not necessarily as a single disease but as a syndrome—a complex of potentially related symptoms that tend to occur together—that may have several causes." Despite the publication of three subsequent case definitions [1–3] and the conduct of hundreds of clinical and epidemiologic studies, no single cause for this debilitating illness has been identified. Furthermore, findings are not consistent across studies. Failure to determine a cause or lack of consistency in findings may reflect heterogeneity in study populations [16], differences in case definitions or different interpretations of the same case definition. The simplest explanation might be that CFS is not yet appropriately defined. In fact, many aspects of CFS are still controversial.

We attempted to address one of the most controversial aspects in defining CFS: Which symptoms, in addition to unexplained chronic fatigue, should be used to identify CFS as a single entity? The 1994 case definition [1] required that at least four of the eight case-defining symptoms be present. We used factor analysis to identify symptom dimensions (i.e., factors) of unexplained chronic fatigue; in particular, to investigate whether the 1994 CFS case-defining symptoms would be included in a single dimension of unexplained chronic fatigue. Our results revealed that unexplained chronic fatigue was multidimensional and that CFS symptoms were not included in a single dimension. CFS symptoms, except severe headaches (dropped early in the analysis), were distributed across the factors (musculoskeletal, infection and cognition–mood–sleep). Thus, CFS is also multidimensional, and it overlaps with other dimensions of unexplained chronic fatigue. The general answer to the above question is that it might not be possible to use symptoms to define CFS as a single entity.

Multiple dimensions of CFS have also been identified in a study in which principal components analysis and latent class analysis of symptoms among CFS subjects [17] were used to identify two patient groups: one reporting symptoms of somatoform disorders and the other reporting neuropsychological symptoms. These two patient groups were clinically heterogeneous and the authors suggested different etiologies for each group. Another study identified three principal components defining cognitive problems, flu-like symptoms and neurologic symptoms [18]. Two recent literature reviews on this subject concluded that there is substantial overlap between CFS symptoms and symptoms of other unexplained chronic illnesses [19,20]. Finally, a study in a primary care setting also demonstrated the overlap of CFS symptoms in other forms of unexplained chronic fatigue [21]. Additional work is needed to incorporate symptom multidimensionality and overlap with other illnesses into CFS diagnosis and etiology.

As a second objective, we estimated scores from the factor analysis model to measure chronic unwellness associated

with each factor. CFS subjects, when compared with chronic fatigue subjects with insufficient CFS criteria, had higher scores in all three factors. Although there was some overlap between the score distributions, none of the non-CFS subjects had higher scores than the maximum score among persons with CFS. This finding suggests that CFS may represent the end of the chronic unwellness spectrum, at least with respect to symptomatology.

We also provided two applications for factor scores. In the first application, we performed cluster analysis to assign subjects to distinct subgroups. Three clusters largely differed from the original fatiguing illness subgroups. In fact, the kappa statistic of .0083 indicates poor agreement between the original and the cluster classifications. Consistent with the analysis of individual factor scores that indicated overlap among groups of subjects with fatiguing illnesses, most CFS subjects (79%) were assigned to the third cluster, together with most CFS-like subjects (73%) and a few of the CF subjects (21%). We offer two explanations for this finding: (1) some subsets of CF subjects might be as chronically unwell as CFS or CFS-like subjects and therefore might need to be considered in the diagnosis CFS, and (2) chronic unwellness levels per se are not sufficient to discriminate CFS (or CFS-like) subjects from subjects with less severe disease. Therefore, other measurements need to be considered to make the CFS classification more specific. This idea follows the work of Wessely et al. [19] who suggested that the relevant parameters for classifying medically unexplained illnesses include number and duration of symptoms, subject's attributions for the symptoms and physiological and psychological measurements. In the second application for factor scores, we proposed that scores be used as stratifying variables when determining the association between risk factors and CFS. An example using scores dichotomized into values below and above the 75th percentile of the overall distribution revealed the differential effect of sex, a known risk factor for CFS, in each stratum.

Two other population-based studies of fatiguing illness in the United States have used factor analysis of symptoms. The first study [22] conducted in San Francisco also identified three factors. However, factor composition was quite different from that in the present study and a musculoskeletal dimension was not detected. The second, more recent, study in Chicago [23] detected four factors. There was some overlap with our musculoskeletal and cognition–mood–sleep factors. These inconsistencies likely reflect the use of different sets of symptoms, the application of distinct factor analysis models (e.g., dichotomous factor vs. common factor) and different populations. In the current study, we only focused on subjects with unexplained chronic fatigue. The other studies combined fatigued and non-fatigued subjects [22], or considered subjects with explained and unexplained fatigue [23]. Of interest, a cluster analysis of data from the Chicago study [24] identified three clusters that share similar characteristics to the clusters identified in our analysis (e.g., a single cluster that includes the most unwell individuals and the highest proportion of CFS subjects).

Our findings are limited by the number and type of symptoms used in the analysis. It is well established that factor structures depend on the variables included in the factor analysis model [10]. We suggest that further studies to identify dimensions of unexplained chronic fatigue should consider using a more comprehensive and standardized symptoms questionnaire. Another limitation of our study concerns the estimation of factor scores, which was performed using a complex algorithm that weighted symptoms according to the dichotomous factor model. If appropriate statistical software is available (such as the one used in our study), factor scores can be calculated for any other sample by defining the factor model and fixing all parameters to the values estimated in our sample. A simpler alternative to model-based scores is to assign unit weights to the symptoms with primary loadings on each factor and take the sum of the reported symptoms (e.g., sum of reported musculoskeletal symptoms, infection symptoms and mood–cognition–sleep symptoms) as the score [10]. Unit weighting scores are almost as efficient as the model-based scores [25] and are usually highly correlated with model-based scores [10]. In our study, the correlations were .92, .93 and .94 for the first, second and third factors, respectively.

In summary, dichotomous factor analysis of symptoms suggests that CFS, as currently defined [1], is a multidimensional symptomatic phenomenon overlapping with other syndromes of unexplained chronic fatigue. This concept must be considered in further research to refine the definition of CFS and determine the etiology of the syndrome. Finally, knowing the degree of chronic unwellness due to each dimension might be useful in assigning subjects to distinct categories or in stratifying subjects to assess the effect of potential risk factors on CFS.

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