

Factor Analysis of Unexplained Severe Fatigue and Interrelated Symptoms

Overlap with Criteria for Chronic Fatigue Syndrome

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The objective of this study was to identify factors explaining the correlations among unexplained severe fatigue of different durations (1–5 months or ≥ 6 months) and symptoms reported as being significant health problems during a preceding 4-week period. Between June and December of 1994, a cross-sectional, random digit dialing telephone survey was conducted among residents of San Francisco, California. All subjects who reported having severe fatigue lasting for ≥ 1 month and a random sample of nonfatigued subjects were asked to participate in a detailed telephone interview. Data from 1,510 individuals aged 18–60 years who did not have medical or psychiatric conditions that could explain their severe fatigue were analyzed. Common factor analyses identified three correlated factors (defined as “fatigue-mood-cognition” symptoms, “flu-type” symptoms, and “visual impairment”) that explained the correlations among fatigue lasting for ≥ 6 months and 14 interrelated symptoms. No factor explained the correlations among fatigue lasting for 1–5 months and other symptoms. The combination of fatigue of ≥ 6 months’ duration and selected symptoms overlaps with published criteria used to define cases of chronic fatigue syndrome (CFS). Although symptoms described in this study were reported as appearing within the preceding month, and CFS symptoms must have been present for the previous 6 months, these results provide empirical support for the interrelations among unexplained fatigue of ≥ 6 months’ duration and symptoms included in the CFS case definition. *Am J Epidemiol* 1998;148:72–7.

cross-sectional studies; factor analysis, statistical; fatigue; fatigue syndrome, chronic

Chronic fatigue syndrome (CFS) is a severely disabling illness characterized by persistent or relapsing chronic fatigue of at least 6 months’ duration that is not the result of ongoing exertion, is not alleviated by rest, and results in substantial reduction of previous occupational, social, educational, or personal activities (1). In addition, to be diagnosed as having CFS, patients must report at least four of the following eight symptoms as having been concurrently present for at least 6 months: impaired memory or concentration, sore throat, tender cervical or axillary lymph nodes, muscle pain, pain in multiple joints, incident headaches, unrefreshing sleep, and postexertion malaise. No objective physical or laboratory signs have been identified for CFS, and no symptom is specific to the illness. Thus, CFS is an exclusionary diagnosis that is

made only after a thorough clinical evaluation for identification of other medical or psychiatric causes that might account for the chronic fatigue.

The current case definition of CFS is based on a consensus opinion of 24 internationally recognized experts in CFS research (1). It was derived from their knowledge and clinical experience with patients who were sick enough to visit a physician and who had sufficient resources to do so, and it was not based on analytical data. Controversy exists over exactly which symptoms, if any, must be included to make the definition more specific (2). Population-based studies exploring which symptoms accompany fatigue lasting for ≥ 6 months would help to resolve this controversy. Such studies would have to demonstrate, empirically, that CFS case-defining symptoms are simultaneously correlated with unexplained severe, debilitating fatigue of ≥ 6 months’ duration.

This investigation used information from a population-based study of self-reported fatigue in San Francisco, California (3), to conduct an analysis of correlations among unexplained severe fatigue of differing durations and symptoms that had been reported as significant health problems in the preceding 4 weeks. The objective was to identify the underlying factors ex-

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Abbreviation: CFS, chronic fatigue syndrome.

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plaining the correlations among symptoms and unexplained severe fatigue lasting for 1–5 months and ≥ 6 months. Results were compared with criteria specified in the CFS case definition.

MATERIALS AND METHODS

Design

A random digit dialing survey was carried out in San Francisco (3) to estimate the prevalence of unexplained severe, prolonged (≥ 1 month) fatigue and unexplained severe, chronic (≥ 6 months) fatigue in the population. Between June 1 and December 1 of 1994, a random sample of 8,004 residential households was selected, and 16,970 household members were screened through a telephone interview. Information on age, sex, race/ethnicity, and the presence of fatigue was obtained. All subjects responding positively to the questions “Are you suffering from severe fatigue, extreme tiredness, or exhaustion?” and “Has this fatigue been present for a period of 1 month or longer?” and a random sample of the nonfatigued individuals were asked to participate in a more detailed telephone interview. Overall response rates, which were not significantly associated with sex, race/ethnicity, or age, were 89 percent and 83 percent for fatigued and nonfatigued subjects, respectively (3). Participants were asked whether any of 30 symptoms had been a significant health problem during the previous 4 weeks. Information was gathered on the onset of fatigue and on other medical or psychiatric conditions that could explain severe fatigue lasting for 6 months or longer.

Subjects

We included respondents aged 18–60 years who had no exclusionary medical or psychiatric conditions (1) that could explain severe fatigue. The exclusionary conditions included self-reported alcohol dependency, anemia, anorexia/bulimia, cancer, chronic bronchitis, hepatitis, diabetes mellitus, heart disease, hypothyroidism, immune deficiency disease, systemic lupus erythematosus, manic-depressive disorder, multiple sclerosis, rheumatoid arthritis, schizophrenia, stroke, surgery, or pregnancy in the year prior to interview. Eligible subjects were classified as either 1) fatigued for 1–5 months; 2) fatigued for ≥ 6 months; or 3) not fatigued.

Symptoms

Subjects were asked whether any of the following 30 symptoms had been a significant health problem during the previous 4 weeks: sore throat, tender lymph

nodes, mouth sores or fever blisters, rash, nausea, diarrhea, constipation, stomach or abdominal pain, inability to tolerate alcohol, unusual sensitivity to certain foods, sinus or nasal symptoms, general weakness, unusual fatigue following exertion, shortness of breath, numbness or tingling, muscle aches or muscle pain, pain in joints, feverishness, chills, night sweats, excessive sleeping, problems getting to sleep or waking up early in the morning, severe headaches, dizziness, photophobia, seeing spots, visual disturbances, forgetfulness or memory problems, difficulty thinking or concentrating, and depression. Valid responses to the questions were “yes,” “no,” “don’t know,” and “refused.” Data for persons who declined to respond were treated as missing. Data coded as “don’t know” were treated as negative responses, because we assumed that if a symptom had been present at a significant level during the previous 4 weeks, the subject would have remembered it and answered positively.

Statistical analyses

We used common factor analysis (4), a relatively simple and flexible statistical tool, to identify underlying relations among symptom data. Two variables were created to contrast unexplained severe fatigue of different durations with the absence of fatigue. The first variable was coded as 1 if unexplained severe fatigue had lasted for 1–5 months and 0 if fatigue was not present. The second variable was coded as 1 if unexplained severe fatigue had persisted for ≥ 6 months and 0 if fatigue was not present. The other 30 symptoms were coded as 1 if present or 0 if absent. The Pearson correlation matrix was constructed and correlations were computed. Symptoms that did not have at least one correlation of ≥ 0.30 were eliminated, because it was likely that such items would perform poorly in a factor analysis (5).

We subjected the correlation matrix to two common factor analyses; one included only subjects who had been fatigued for ≥ 6 months and those who were not fatigued; the other included only subjects who had been fatigued for 1–5 months and those who were not fatigued. The unweighted least squares method (4) with squared multiple correlations in the diagonal was used, and the number of factors was determined by specifying that 100 percent of common variance should be accounted for by the retained factors, using the squared multiple correlations. To facilitate interpretation, we rotated the retained factors using the promax oblique procedure, which extracts correlated factors. The interfactor correlations were computed, and the rotated factor pattern was examined to determine whether an oblique rotation yielded a simple structure (i.e., high factor loadings in only one factor).

Symptoms were retained for further analyses if they had factor loadings of ≥ 0.35 in only one factor (4, 6). These symptoms provided the final factor analysis solution. Proportions were compared by chi-squared test. All analyses were performed using SAS software (SAS Institute, Inc., Cary, North Carolina).

RESULTS

Of the 1,810 respondents aged 18–60 years, 1,733 (95.7 percent) had complete data on all 30 symptoms and on fatigue duration. A total of 1,078 subjects did not report fatigue, and 655 reported current fatigue of at least 1 month's duration. Among the fatigued individuals, 177 reported having been fatigued for 1–5 months, 255 reported having had unexplained fatigue for at least 6 months, and 223 reported having had fatigue for ≥ 6 months that could be explained by a medical or psychiatric condition. After subjects with explainable fatigue were excluded, the final sample for analysis consisted of 1,510 respondents (71.4 percent not fatigued, 11.7 percent fatigued for 1–5 months, and 16.9 percent fatigued for ≥ 6 months).

No significant differences were found between non-fatigued and fatigued subjects with respect to age or race/ethnicity, but there were significantly more females among those who had been fatigued for ≥ 6 months than among those who were not fatigued (χ^2 test: $p < 0.01$) (table 1). The prevalence of the 30 symptoms among the three groups of participants (not fatigued, fatigued for 1–5 months, and fatigued for ≥ 6 months) is shown in table 2. All symptoms were significantly more prevalent among fatigued subjects (≥ 6 months or 1–5 months) than among nonfatigued

subjects ($p = 0.001$ in the χ^2 test for each comparison). However, the prevalence of symptoms did not differ significantly between the fatigue groups, except for photophobia and seeing spots (χ^2 test: $p = 0.040$ and $p = 0.049$, respectively). Problems getting to sleep, general weakness, muscle aches and pain, difficulty thinking or concentrating, depression, and unusual fatigue after exertion were the most prevalent (>50 percent) symptoms in both fatigue categories.

Almost all symptoms had at least one correlation with another symptom that was above 0.30; the exceptions were mouth sores, rash, constipation, alcohol intolerance, unusual food sensitivity, and sleeping excessively (the largest correlations were 0.21, 0.20, 0.26, 0.23, 0.29, and 0.27, respectively). These symptoms were dropped from subsequent factor analyses.

Three factors were extracted from the first common factor analysis, which included subjects who had been fatigued for at least 6 months and those who were not fatigued. Being fatigued for ≥ 6 months and 14 other symptoms had factor loadings of ≥ 0.35 in only one factor (data not shown). These symptoms were resubmitted to factor analysis and rotated to a three-factor solution (table 3). The first factor, which we labeled "fatigue-mood-cognition," consisted of fatigue for ≥ 6 months, general weakness, unusual fatigue postexertion, difficulty thinking or concentrating, forgetfulness, problems getting to sleep, and depression. The second factor, which we called the "flu-type" factor, consisted of feverishness, chills, sore throat, tender lymph nodes, and night sweats. The third factor, "visual problems," consisted of visual disturbances, seeing spots, and photophobia. The interfactor correlations were mild to moderate (0.38–0.55), and the oblique factor pattern was closer to simple structure than the orthogonal factor pattern (which assumes uncorrelated factors). Thus, we decided that an oblique rotation yielded the best solution.

The second factor analysis, which included subjects who had been fatigued for 1–5 months and those who were not fatigued, yielded two factors (table 4). Nineteen symptoms had loadings of ≥ 0.35 in only one factor (the factor loading for general weakness was 0.39 in both factors). Unexpectedly, severe fatigue for 1–5 months failed to load in any of the factors at the 0.35 cutoff point. In the final solution, factor 1 comprised the symptoms of forgetfulness, difficulty thinking, depression, unusual fatigue postexertion, shortness of breath, problems getting to sleep, joint pain, muscle pain, numbness, visual disturbances, seeing spots, photophobia, dizziness, severe headaches, and diarrhea (factor loadings = 0.70, 0.62, 0.50, 0.34, 0.38, 0.44, 0.37, 0.37, 0.41, 0.60, 0.53, 0.48, 0.40, 0.40, and 0.26, respectively); and factor 2 comprised

TABLE 1. Age, sex, and race distributions (%) of non-fatigued subjects and subjects reporting being fatigued for 1–5 months and ≥ 6 months, San Francisco, California, 1994

	Nonfatigued (n = 1,078)	Fatigued		p value
		1–5 months (n = 177)	≥ 6 months (n = 255)	
Age (years)				
<30	36.3	31.1	30.6	0.147
30–39	27.1	33.3	35.3	
40–49	22.2	23.2	20.4	
50–60	14.5	12.4	13.7	
Mean	35.5 (11.1)*	36.0 (10.4)	35.9 (10.0)	
Female sex	50.8	55.3	61.6	0.007
Race/ethnicity				
White	48.3	44.1	45.9	0.493
Black	10.0	14.1	11.8	
Other	41.7	41.8	42.4	

* Numbers in parentheses, standard deviation.

TABLE 2. Prevalence (%) of selected symptoms among nonfatigued subjects and subjects reporting being fatigued for 1–5 months and ≥6 months, San Francisco, California, 1994

Symptom	Nonfatigued (n = 1,078)	Fatigued*		p value†
		1–5 months (n = 177)	≥6 months (n = 255)	
Problems getting to sleep	24.3	58.2	65.5	0.123
General weakness	12.2	70.6	62.4	0.075
Muscle aches or pain	29.1	69.5	60.4	0.052
Difficulty thinking or concentrating	15.7	57.6	59.6	0.681
Depression	17.5	62.2	55.7	0.180
Unusual fatigue postexertion	9.1	53.7	53.3	0.945
Sinus or nasal symptoms	27.3	49.2	49.8	0.894
Pain in joints	19.5	44.1	47.8	0.439
Stomach or abdominal pain	15.4	47.5	45.1	0.628
Forgetfulness or memory problems	13.0	40.1	44.7	0.343
Severe headaches	13.8	35.6	43.5	0.098
Eyes extremely sensitive to light	11.9	31.1	40.8	0.040
Sore throat	13.9	36.7	37.3	0.910
Shortness of breath	10.1	40.1	36.9	0.494
Sleeping excessively	12.2	36.2	35.7	0.920
Nausea	8.0	35.6	35.3	0.949
Dizziness	7.3	35.6	31.4	0.359
Numbness or tingling	8.3	33.9	31.0	0.523
Chills	6.8	29.4	29.4	0.994
Diarrhea	10.5	33.9	28.2	0.209
Night sweats	8.3	30.5	28.2	0.609
Feverishness	6.2	27.7	24.7	0.487
Unusual sensitivity to certain foods	8.2	23.2	24.7	0.712
Constipation	8.3	22.0	22.4	0.937
Tender lymph nodes	5.1	18.1	22.0	0.325
Visual disturbances	6.8	21.5	20.4	0.786
Seeing spots	4.7	12.4	19.6	0.049
Mouth sores or fever blisters	8.1	16.4	19.2	0.452
Rash	7.1	21.5	16.9	0.228
Inability to tolerate alcohol	4.7	13.6	13.7	0.961

* χ^2 tests comparing the prevalence of each symptom in all fatigued subjects with that in nonfatigued subjects yielded a p value of 0.001 for each comparison.

† χ^2 test comparing the prevalence of the symptom in persons who were fatigued for 1–5 months with that in persons who were fatigued for ≥6 months.

feverishness, chills, sore throat, and tender lymph nodes (factor loadings = 0.71, 0.56, 0.46, and 0.46, respectively). The interfactor correlation was 0.60.

DISCUSSION

In this study, factors explaining the correlations among unexplained severe fatigue and symptoms that had been significant health problems in the 4 weeks preceding the subject's interview depended on the duration of fatigue. Using common factor analysis and predetermined statistical criteria, we identified a factor composed of fatigue of ≥6 months' duration and mood-cognition symptoms which was moderately correlated with a "flu-type" factor and a "visual problems" factor. In contrast, no factor seemed to explain the correlations between unexplained severe fatigue of 1–5 months' duration and any of the other symptoms.

Common factor analysis is used to explain the correlations among measured variables, and it is used as

a means of identifying "the underlying dimensions of a domain of functioning, as assessed by a particular measuring instrument" (4, p. 286). In this study, the particular measuring instrument was the inventory of 30 symptoms and self-reported fatigue, and the domain of functioning was fatiguing illness in the San Francisco population. When this instrument was used, the first and most important dimension within this domain was the factor including fatigue for ≥6 months and mood-cognition symptoms. The second and third dimensions, which correlated with the first, indicated that subjects with many fatigue-mood-cognition symptoms were likely to experience many influenza-like symptoms or visual problems.

Failure of some symptoms to be part of any dimension (i.e., those symptoms that did not load in any factor) might reflect the heterogeneity of the symptoms with respect to the domain being studied. It is possible that these symptoms belong to a completely

TABLE 3. Results of factor analysis (factor loadings $\times 100$) of unexplained severe fatigue lasting for ≥ 6 months and 14 symptoms reported as being significant health problems in the preceding 4 weeks, San Francisco, California, 1994*

Symptom	Factor 1	Factor 2	Factor 3
Difficulty thinking or concentrating	74	-3	5
Depression	61	-2	3
General weakness	60	21	-3
Unexplained severe fatigue for ≥ 6 months	57	15	-7
Forgetfulness or memory problems	53	-11	27
Unusual fatigue postexertion	49	22	-1
Problems getting to sleep	47	6	5
Feverishness	-6	73	2
Chills	2	59	6
Sore throat	16	37	-2
Tender lymph nodes	15	36	-5
Night sweats	8	36	16
Visual disturbances	0	-3	70
Seeing spots	1	8	58
Eyes sensitive to light	20	12	33

* Interfactor correlations were 0.55, 0.54, and 0.38 between factor 1 and factor 2, between factor 1 and factor 3, and between factor 2 and factor 3, respectively.

different health domain. It was surprising that being fatigued for 1–5 months was not associated with any of the factors derived in the analysis, despite its univariate correlations with several symptoms. One explanation might simply be that fatigue lasting for 1–5 months is not part of the same pathology generated by other symptoms present in the previous 4 weeks.

These findings are important, because they suggest that as unexplained severe fatigue progresses in time (and 6 months might be the threshold), other “natural” accompanying symptoms are likely to arise. This concept is not new. What is new is the empirical evidence supporting it. The CFS case definition was based on the concept that unexplained severe fatigue of ≥ 6 months’ duration (and not fatigue of 1–5 months’ duration) tends to occur together with related symptoms (7). Based on their clinical experience with fatigued patients, a panel of international experts has agreed that a case of CFS is defined by the presence of unexplained severe fatigue of ≥ 6 months’ duration and the concurrent appearance of at least four of eight related symptoms (1). Thus, without formally labeling it, the researchers created a measuring instrument (or a scale) composed of eight CFS case-defining symptoms and were using a cutoff point of four symptoms to define cases. They did not, however, provide empirical support for the hypothesized interrelations among unexplained severe fatigue of ≥ 6 months and the eight symptoms.

In our study, we assumed a broader scope and range

TABLE 4. Results of factor analysis (factor loadings $\times 100$) of unexplained severe fatigue lasting for 1–5 months and 24 symptoms reported as being significant health problems in the preceding 4 weeks, San Francisco, California, 1994*

Symptom	Factor 1	Factor 2
Forgetfulness or memory problems	65	-10
Difficulty thinking or concentrating	62	7
Visual disturbances	60	-18
Depression	53	12
Seeing spots	48	-7
Numbness or tingling	47	8
Muscle pain	41	13
Eyes sensitive to light	40	7
Problems getting to sleep	40	13
Dizziness	38	27
Joint pain	37	8
Shortness of breath	37	22
Severe headaches	36	14
Diarrhea	35	14
Night sweats	31	20
Feverishness	-8	67
Sore throat	-8	54
Tender lymph nodes	-12	53
Chills	9	50
Unusual fatigue postexertion	29	35
General weakness	39	39
Nausea	27	33
Unexplained severe fatigue for 1–5 months	29	32
Stomach pain	24	31
Sinus or nasal symptoms	14	31

* The interfactor correlation between factor 1 and factor 2 was 0.65.

of the fatigue domain and attempted to identify its dimensions on the basis of data from a random sample of the San Francisco population. The first two correlated dimensions included five symptoms that overlapped with CFS case-defining symptoms: difficulty thinking and concentrating, unusual fatigue postexertion, and problems getting to sleep in factor 1, and sore throat and tender lymph nodes in factor 2. These findings suggest that the scale used for classification of CFS cases might be viewed as a combination of underlying dimensions of a general fatigue construct. Although symptoms in this study were reported as appearing during the month preceding the subject’s interview, and CFS symptoms must have been present for the previous 6 months, these results provide empirical support for the hypothesized interrelations among unexplained severe fatigue of ≥ 6 months’ duration and most of the CFS case-defining symptoms.

This study of a city’s population is also important because the fatigue-mood-cognition factor we identified was similar to that found in a recent study of military personnel (“A Chronic Multisymptom Illness affecting Persian Gulf War Veterans”) conducted by the Centers for Disease Control and Prevention (unpublished manuscript). Approximately 4,000 subjects

(86 percent of them male) stationed at four military bases were surveyed, and factor analysis was used to identify patterns in the correlations among 35 symptoms (almost identical to the ones included in this study). Correlations among symptoms present for ≥ 6 months yielded two factors. The first factor consisted of depression, anxiety, moodiness, memory problems, fatigue, trouble with words, and sleeping problems. The second factor consisted of muscle pain, joint stiffness, and joint pain. The similarity between the first factors identified in both this study and the military study, despite the differences in sex prevalence and sampling populations, suggests that the fatigue-mood-cognition dimension of health is consistent across different segments of the general population.

Several limitations of this study must be considered. First, we used common factor analysis as an exploratory tool to identify and describe patterns of interrelations, but we were unable to cross-validate or confirm our results. Second, we used a linear factor analysis model for the analysis of dichotomous symptom data, and this approach may have resulted in biased estimates of factor loadings (4). Third, we used self-reported symptom data that could not be confirmed. Thus, we recognize that some level of misclassification is present in the data. It is also possible that fatigued subjects, especially those who were severely ill, might have recalled more symptoms than nonfatigued subjects. Finally, since symptom data were evaluated only for the previous month and information was inadequate to accurately assess the number of CFS cases in the sample, it was not possible to directly compare the current CFS case definition with a definition derived solely from the factor analysis.

The strength of this study is that it provides the first empirical evidence suggesting that the symptoms included in the CFS case definition may represent true correlates of fatigue. Our findings indicate that the symptom complex consisting of fatigue lasting for ≥ 6 months and mood-cognition and flu-type symptoms is not an artificial construct. Nevertheless, additional study of the interrelations between fatigue and selected symptoms is warranted.

In summary, we have shown that a statistical approach generally used in psychology or psychiatry to reveal dimensions of personality or behavior (8) was useful in identifying three correlated dimensions of health in the San Francisco population: fatigue-mood-cognition, flu-like symptoms, and visual impairment. Further studies are needed to replicate our findings and

to demonstrate that empirical evidence supports the interrelations among unexplained severe, chronic fatigue and symptoms included in the current CFS case definition. In such studies, subjects should be clinically evaluated, and more detailed information on symptom duration should be collected. In addition, if a sufficient number of subjects is accrued, a dichotomous exploratory (9) and confirmatory (10) factor analysis should be performed, using half of the sample to generate hypotheses about the factor structure and the other half to test the hypotheses. Such an analysis would make it possible to examine changes (e.g., the elimination or inclusion of symptoms (2)) in the current CFS case definition. Finally, cluster analysis might be used to determine whether CFS cases define heterogeneous groups, indicating consistency of findings with similar results reported in the literature (11).

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