

Functional Status, Neuropsychological Functioning, and Mood in Chronic Fatigue Syndrome (CFS)

Relationship to Psychiatric Disorder

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Individuals with chronic fatigue syndrome (CFS) face chronic physical debilitation, reduced neuropsychological functioning, and changes in emotional well-being that significantly detract from quality of life. The role of psychiatric disturbance in reducing quality of life in CFS remains unclear. In the current investigation, the role of psychiatric status in reducing health-related quality of life in CFS was examined. Four subject groups were compared on measures of functional well-being, mood, and neuropsychological status: individuals with CFS and no history of psychiatric illness, individuals who had current symptoms of psychiatric illness that began after their CFS diagnosis, individuals who had current symptoms of psychiatric illness that began before their CFS diagnosis, and a healthy sedentary control group. Overall, it was found that individuals with CFS suffer from profound physical impairment. Concurrent psychiatric illness, however, did not adversely affect physical functional capacity. Physical functional capacity was not worse in individuals with a concurrent psychiatric illness. As expected, concurrent psychiatric illness was found to reduce emotional well-being. Moreover, individuals with a psychiatric illness that predated the onset of CFS suffered the greatest emotional distress. Thus, an individual's psychiatric history should be considered when attempting to understand the factors maintaining disability in CFS.

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Individuals with chronic fatigue syndrome (CFS) have a significantly reduced quality of life because of neuropsychological dysfunction, physical decline, and emotional distress (Bombardier and Buchwald, 1996; Buchwald et al., 1996; Komaroff et al., 1996; Moss-Morris et al., 1996; Myers and Wilks, 1999; Natelson et al., 1995; Schweitzer et al., 1995; Tiersky et al., 1997). This impairment in quality of life, in conjunction with fatigue, is tightly linked with disability (Fischler et al., 1997; Wagner-Raphael et al.,

1999). This disability extends across broad areas of human functioning, but those of social and role functioning are the most impaired (Anderson and Ferrans, 1997; Bombardier and Buchwald, 1996; Buchwald et al., 1996; Komaroff et al., 1996; Natelson et al., 1995; Schweitzer et al., 1995). It is clear that CFS can result in profound and pervasive debilitation. How fatigue and neuropsychological, physical, and psychiatric factors influence this disability remains unclear.

Emotional disturbance may be one of the most significant contributors to disability in CFS. Psychiatric disturbance is frequently observed in CFS (Wessely et al., 1998) and is known to contribute to significant impairment in functional status in individuals with other medical conditions (Fifer et al., 1994; Katon, 1996; Katon and Sullivan, 1990; Levenson et al., 1990; Sherbourne et al., 1996). Indeed, this double illness burden phenomenon is well documented. However, the studies that have examined whether psychiatric disturbance contributes to decreased functional status and neuropsychological dysfunction in CFS have found this not to be the case (Christotodoulou et al., 1998; Komaroff et al.,

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1996; Tiersky et al., 2000; Wagner-Raphael et al., 1999). Quite simply, based on these studies, comorbid psychiatric illness does not appear to result in further reduced quality of life in CFS. This is surprising given the consistency of the literature noted above.

Methodological limitations inherent to the studies by Komoroff et al. (1996), Tiersky et al. (2000), and Wagner-Raphael et al. (1999) may account for the lack of expected findings. One limitation of the study by Komoroff et al. (1996) is that the subjects were not necessarily suffering from a current depressive illness that would actively affect their functional status. The study by Tiersky et al. (2000) was limited by small sample sizes that may have compromised power, thereby leading to little chance of finding significant group differences. The third study used patients who did not all fulfill the case definition for CFS; this added heterogeneity in the subject pool might have obfuscated an effect of comorbid psychiatric illness (Wagner-Raphael et al., 1999). Thus, limited conclusions can be drawn from these investigations.

Moreover, although some attempt has been made to examine the effects of psychiatric disturbance on functional capacity in CFS, no study has specifically examined the effects of long-standing psychiatric illness on functional well-being. Again, this is an important question because chronic or severe psychiatric conditions can lead to a reduced quality of life in patients with (Keitner et al., 1991; Levenson et al., 1990) and without (Hays et al., 1995; Spitzer et al., 1995; UK700 Group, 1999; Warner and Huxley, 1993) comorbid major medical illness. Long-standing psychiatric illness may be related to even greater reductions in quality of life than psychiatric disturbances that develop after the onset of CFS, because they reflect a history of more chronic maladaptation. When examining the effects of psychiatric illness on functional well-being or quality of life in CFS, therefore, it is important to examine the effects of chronic and acute psychiatric disturbances.

Despite some disagreement in the literature, some evidence suggests that psychiatric illness that develops after the onset of CFS affects neuropsychological function in CFS (DiPino and Kane, 1996; Michiels et al., 1996; Moss-Morris et al., 1996; Tiersky et al., 1997; Volmer-Conna et al., 1997; Wearden and Appleby, 1997). However, the findings in this area also seem somewhat anomalous. Specifically, DeLuca et al. (1997) found that individuals with CFS who never suffered from a psychiatric illness showed greater neuropsychological impairment than those people who developed a psychiatric disorder after their CFS onset. Moreover, in a related

investigation, Lange et al. (1999) found that patients with CFS with no psychiatric history showed more white matter lesions on brain magnetic resonance imaging, suggesting greater neurological involvement in those individuals with no psychiatric history. The counterintuitive finding by DeLuca et al. (1997) suggests that contrary to what may be expected, psychiatric disorders beginning after CFS onset do not appear to affect neuropsychological performance adversely. This may be due to greater neurological involvement in the group with no psychiatric history.

Most studies that have investigated the relationship between neuropsychological performance and psychiatric status in CFS do not specify the duration of the psychiatric illness or have looked at only psychiatric disturbances after CFS onset (DiPino and Kane, 1996; Moss-Morris et al., 1996; Tiersky et al., 1997). This may explain some of the discrepancy in the literature regarding the effects of psychiatric status on neuropsychological functioning. For instance, increased severity and chronicity of illness are related to reduced neuropsychological functioning in individuals with psychiatric disorders (Martinez-Aran et al., 2000; McKay et al., 1995). Chronic psychiatric illness therefore may affect neuropsychological functioning adversely in CFS. Subjects with this sort of history may have been included in the studies that, unlike that by DeLuca et al. (1997), found that psychiatric illness leads to reduced neuropsychological functioning in CFS. It is important to determine whether duration of psychiatric illness affects neuropsychological functioning in CFS, because this may explain the variability in studies and be an important stratification variable for future investigations.

The purpose of this study was to evaluate the effect of psychiatric illness on functional well-being and neuropsychological functioning in CFS. There were six specific hypotheses: 1) If functional decline is primarily a result of psychiatric disturbance, individuals with CFS and a psychiatric disorder will be more impaired across measures of functional status and well-being than individuals with CFS and no psychiatric disorder and the latter group will not differ from the healthy group; 2) If psychiatric illness results in a double illness burden, subjects suffering from comorbid psychiatric illness will be more impaired than those without psychiatric comorbidity across measures of functional status and well-being; 3) Individuals with psychiatric disorders predating their CFS onset will show the greatest declines in functional well-being because they may have a chronic history of maladjustment; 4) Individuals with long-standing psychiatric histories predating

their CFS onset will show the most severe neuropsychological deficits; 5) Individuals with a psychiatric history preceding their CFS onset will show the greatest declines on measures of mood, followed by those whose psychiatric disorder developed after the onset of CFS; and 6) Individuals with CFS and no history of psychiatric disturbance will show worse performance on measures of mood than healthy controls.

Methods

Participants

Participants were 107 individuals who met the 1994 CFS case definition (Fukuda et al., 1994). Based on their psychiatric histories, participants were divided into the following three subject groups: the no-psych group, which included 60 individuals who were identified as having CFS, but no history of psychiatric illness; the post-psych group, which included 21 subjects who had a current psychiatric illness that developed after their CFS diagnosis but no history of psychiatric illness that predated the CFS onset; and the pre-psych group, which included 26 subjects who developed a psychiatric illness before their CFS diagnosis and who continued to have that illness currently. A healthy control group included 41 individuals who had no evidence of medical or psychiatric illness.

In addition to meeting the 1994 CFS criteria, all participants also met the following inclusion criteria: onset of CFS within the 15 years before the initial evaluation; no history of substance abuse within the 2 years before study participation; no lifetime history of mania, an eating disorder, or a psychotic disorder; and no loss of consciousness for more than 5 minutes. Healthy individuals met the following inclusion criteria: no evidence of major medical illness on physical examination or noted by self-report, no history of loss of consciousness for more than 5 minutes, no psychiatric history, no use of medication other than birth control pills, and no regular participation in an exercise program.

Procedure

All participants underwent a history and physical examination that was completed by a physician's assistant trained in the diagnosis of CFS. The date of CFS onset was determined during the history and physical examination. In addition, during this evaluation, the severity of each subject's CFS was rated by the clinician using a 6-point scale. The CFS severity category rankings are listed in Table 1. CFS severity was rated based on the following: level of

TABLE 1
CFS Severity Rating Scale

Rating	Definition of Numeric Rating
1	≥ 50% reduction in activity and 7 symptoms rated as at least substantial (<i>Severe CFS</i>)
2	≥ 50% reduction in activity and 4–6 symptoms rated as at least substantial ≤ 50% reduction in activity and 4 or more symptoms rated as at least substantial (at least 3 symptoms rated as very severe)
3	≤ 50% reduction in activity and 4 or more symptoms rated as at least substantial (no more than 2 symptoms may be rated as very severe)
4	≥ 50% reduction in activity (must be at least substantial) and 4 or more symptoms rated less than substantial
5	"Substantial Reduction in Activity" in activity and 4 or more symptoms rated less than substantial

reduction in activity and number and severity of minor symptoms rated from 0 to 5 (0 = symptom is no problem; 3 = symptom is a substantial problem; 5 = symptom is a very severe problem).

In addition, all subjects completed the Quick Diagnostic Interview for the DSM III-R (Q-DIS; Marcus et al., 1990), a structured, computerized diagnostic interview that was administered by trained personnel. Disorders in the following diagnostic categories were evaluated: affective, anxiety, alcohol and psychoactive substance use, psychotic (schizophrenia), and eating. The presence of somatization disorder was not evaluated. Research suggests that the diagnosis of somatization disorder in CFS is of little heuristic value because of the effects of interviewer bias on its evaluation (*i.e.*, whether a symptom is coded as psychiatric or physical; Johnson et al., 1996). We established the date of onset of each psychiatric disorder and whether it currently existed from the subject's self-report. We defined a psychiatric disorder as predated CFS onset if it occurred at any time before the onset of CFS. Finally, we considered a diagnosis to be current if the symptoms of the disorder continued to within 1 year of the date of the evaluation. In addition to determining the presence and absence of each psychiatric disorder, we also examined whether subjects suffered from intermittent psychiatric illness or had a continuous psychiatric history. Psychiatric illness was considered intermittent if there was a period of at least 1 year in which no diagnosis was evident, whereas continuous was defined as suffering from a disorder throughout a given time frame. Table 2 lists psychiatric disorders identified by the Q-DIS.

All participants were administered a battery of neuropsychological measures that included the following: the digit span, block design, and vocabulary subtests of the WAIS-R (Wechsler, 1981); the Paced

TABLE 2
Number and percent of participants suffering from each specific diagnosis

Disorder	Prepsych-Lifetime ^b	Postpsych-Lifetime ^b	Prepsych-past 12 Months ^b	Postpsych-past 12 Months ^b
Depression	21 (80.8%)	15 (71.4%)	17 (65.4%)	11 (52.4%)
Panic	9 (34.6%)	8 (38.1%)	8 (30.8%)	7 (33.3%)
Agoraphobia	8 (30.8%)	1 (4.8%)	8 (30.8%)	1 (4.8%)
Generalized anxiety	8 (30.8%)	4 (19.0%)	6 (23.1%)	4 (19.0%)
Social phobia	6 (23.1%)	0	3 (11.5%)	0
Simple phobia	4 (15.4%)	0	3 (11.5%)	0
PTSD	4 (15.4%)	0	2 (7.7%)	0
Obsessive compulsive disorder	1 (3.8%)	0	1 (3.8%)	0
Alcohol abuse	2 (7.7%)	0	0	0
Substance abuse ^a	2 (7.7%)	0	0	0

^a Substance Abuse refers to abuse of either cannabis, stimulants, sedatives, or cocaine.

^b Percents do not equal one hundred since an individual could suffer from more than one disorder.

Serial Addition Test (Brittain et al., 1991); the Trail Making Test, parts A and B (Reitan and Tarshes, 1959); and the California Verbal Learning Test (Delis et al., 1987). All testing was completed according to standard procedures by trained research assistants or psychologists.

Finally, all subjects completed four paper-and-pencil questionnaires designed to evaluate functional well-being and mood. First, the SF-36 is a multidimensional health status measure that has been used to assess functional status across a large number of medical and psychiatric populations (Ware et al., 1993). The SF-36 is divided into two composite summary subscales that were used in the current investigation: physical composite score and mental composite score. Second, the Profile of Mood States (POMS, past-week version; McNair et al., 1981) provides self-report data on mood. A composite summary score was used in the final analyses. The POMS was used in a previous study of disability in CFS (Natelson et al., 1995). Third, the neuroticism subtest of the NEO PI-R was used. Fourth, the Multidimensional Fatigue Inventory is a fatigue inventory that has been used to assess fatigue in medical populations, including CFS (Smets et al., 1995; Smets et al., 1996). The general fatigue subscale of the Multidimensional Fatigue Inventory was used in the current investigation.

Data Analysis

Data were analyzed using one-way analyses of variance (ANOVAs) across the four groups. Posthoc analyses were completed using the Tukey procedure. Nonparametric Kruskal-Wallis analyses were completed to examine CFS severity. Significance was set at the traditional level of $\alpha = .05$. Given its highly conservative nature, a Bonferroni correction procedure was not completed (Kutner et al., 1996; Manu et al., 1992). Only planned comparisons, which

were designed to address our initial hypotheses, were completed when examining performance of the groups on the neuropsychological measures. On all measures included in the battery, we compared the pre-psych, post-psych, no-psych, and healthy groups. No other group comparisons were completed.

Results

Group Demographics and Illness Characteristics

Overall, there were no significant differences between the groups in mean age ($F[3, 144] = .96, p = .41$) or mean years of education ($F[3, 144] = 1.60, p = .19$). Across groups, there were more women than men, but this difference did not reach statistical significance ($\chi^2 = .67, p = .88$). Overall, subjects with CFS did not differ significantly in illness characteristics. Specifically, the three CFS groups did not differ in CFS severity, whereby severity was classified by categories ranging from 1 (severe) to 7 (not present; $\chi^2 = 1.54, p = .46$). In addition, the groups did not differ in duration of CFS ($F[2, 110] = .95, p > .05$). Demographic data and illness characteristics are summarized in Table 3.

Psychiatric Status

As expected, the duration of psychiatric illness was significantly longer in the pre-psych group than in the post-psych group (duration of illness in months: prepsych mean = 240.7, SEM = 28.3; postpsych, mean = 43.9, SEM = 7.7; $F[1, 45] = 37.19, p < .001$). Moreover, both groups primarily suffered from continuous psychiatric illnesses with no group differences seen on this illness parameter (percentage of individuals suffering from continuous psychiatric illness: pre-psych = 88.5%; post-psych = 95.2%; $\chi^2 = .69, p = .41$). The pre-psych group also expe-

TABLE 3
Demographics and illness characteristics organized by group

	Prepsych	Postpsych	No psych	Control	χ^2/Γ^d
Age ^a	37.9 (2.1)	39.7 (1.9)	36.0 (1.2)	37.9 (1.2)	0.96
Education ^a	14.5 (0.4)	15.4 (0.6)	15.3 (0.3)	14.6 (0.3)	1.60
Gender ^b					
Females	23 (88.5%)	17 (81.0%)	52 (86.7%)	35 (87.5%)	0.67
Males	3 (11.5%)	4 (19.0%)	8 (13.3%)	5 (12.5%)	
CFS severity ^c	2.0	2.0	2.0	N/A	1.54
CFS duration ^a	47.6 (5.5)	55.9 (6.5)	64.0 (9.1)	N/A	0.95

^a Data reported in means and standard error of the means.

^b Gender data reported in frequencies and percentages (within group).

^c CFS severity classified into categories ranging from 1 (severe CFS) to 7 (No CFS present) and reported in median scores.

^d No significant differences observed.

TABLE 4
Performance of the four subject groups on measures of physical and psychological well-being—mean (SEM)

	Prepsych	Postpsych	No psych	Control
SF-36				
Mental Health	36.60 (2.19) ^d	37.13 (2.34) ^d	45.09 (1.30)	54.66 (0.62) ^{a,b,d}
Physical	28.23 (1.24)	29.29 (2.02)	25.04 (0.93)	55.59 (0.71) ^{a,b,d}
POMS				
Tension-Anxiety	17.68 (1.89) ^d	14.52 (1.47) ^c	9.78 (0.78)	4.28 (0.47) ^{a,b,d}
Depression-Dejection	19.60 (2.95) ^{b,c}	12.29 (2.11)	9.38 (1.15)	3.40 (0.65) ^{a,b,d}
Anger-Hostility	11.92 (1.89) ^d	7.62 (1.37)	6.51 (0.86)	3.50 (0.55) ^a
Fatigue-Inertia	18.88 (1.20)	19.90 (1.16)	18.58 (0.77)	2.35 (0.38) ^{a,b,d}
Confusion-Bewilder	13.20 (1.37)	12.52 (1.40)	10.42 (0.64)	2.53 (0.40) ^{a,b,c}
Total Score	74.48 (8.97) ^c	60.76 (6.88)	47.62 (3.68)	-4.45 (2.34) ^{a,b,d}
NEO PI-R				
Total Score	99.46 (5.84) ^{b,d}	75.94 (4.76)	66.64 (2.99)	56.97 (3.49) ^{a,b}
MFI				
General Fatigue	18.33 (0.52)	18.76 (0.38)	18.53 (0.24)	7.59 (0.60) ^{a,b,d}

^a Differs from Prepsych ($p < .001$)^b Differs from Postpsych ($p < .001$)^c Differs from No Psych ($p < .01$)

^d Differs from No Psych ($p < .001$).

rienced more severe psychiatric illness than the post-psych group, as indicated by suffering from a greater number of lifetime psychiatric diagnoses (mean number of lifetime psychiatric diagnoses: prepsych mean = 2.5, SEM = .3; post-psych mean = 1.3, SEM = .1; $F[1, 45] = 12.90$, $p < .01$). In addition, the groups differed in the number of psychiatric diagnoses experienced within the last year (mean number of psychiatric diagnoses in the past year: prepsych mean = 1.9, SEM = .3; post-psych mean = 1.1, SEM = .1; $F[1, 45] = 5.34$, $p < .05$). Table 2 lists a description of the lifetime and current psychiatric diagnoses suffered by the two CFS groups with psychiatric histories.

Physical Well-Being

Mean performance for all groups on the PCS subscale of the SF-36 is presented in Table 4. Significant group differences were found on this measure of physical functional ability ($F[3,144] = 183.53$, $p < .001$). As expected, the healthy controls outperformed all three of the CFS groups on this measure

($p < .001$). No other significant group differences were observed.

Psychological Well-Being

Table 4 presents the mean performance for all groups on the measures of psychological well-being, the MCS of the SF-36. Significant differences were also found across groups ($F[3,144] = 27.82$, $p < .001$). The healthy control group showed significantly higher scores than all three of the CFS groups (all p values $< .001$), indicating greater emotional well-being. Moreover, as expected, the no-psych group significantly outperformed the pre-psych ($p < .001$) and post-psych ($p < .01$) groups on the MCS, again indicating greater psychological well-being in this group than in the other CFS groups. No other significant group differences were found.

Examination of subjects' performances on the POMS showed findings similar to those of the SF-36 MCS subscale. Once again, significant differences were found across groups ($F(3, 137) = 47.24$, $p < .001$) on the POMS composite score. Healthy con-

TABLE 5
Performance of the four subject groups on neuropsychological measures—mean (SEM)

	Prepsych	Postpsych	No psych	Control
PASAT Total	104.79 (8.56)	130.00 (10.69)	122.47 (4.88)	125.34 (5.74)
Vocabulary ^b	11.25 (0.75)	11.55 (0.90)	11.78 (0.56)	11.20 (0.38)
DS Forward ^{b,c}	7.21 (0.50)	9.55 (0.53) ^a	9.30 (0.33) ^a	9.00 (0.32) ^a
DS Backward ^{b,c}	7.14 (0.53)	8.09 (0.67)	7.06 (0.41)	6.90 (0.33)
Trails A	37.21 (4.58)	29.55 (2.43)	27.28 (1.29) ^a	26.64 (1.40) ^a
Trails B	78.50 (10.73)	59.55 (6.07)	56.72 (2.35) ^a	60.21 (3.47) ^a
CVLT (1–5)	13.07 (0.77)	12.55 (0.93)	13.21 (0.35)	13.20 (0.28)
CVLT SDFR	11.71 (1.08)	10.91 (0.92)	12.06 (0.39)	11.71 (0.41)
CVLT LDFR	12.14 (0.87)	11.36 (0.75)	12.61 (0.44)	12.17 (0.35)

^a Differs from Prepsych ($p < 0.05$)

^b Subtests from the Wechsler Adult Intelligence Scale Revised

^c DS refers to Digit Span.

trols had scores significantly lower than those of all other groups, indicating less emotional distress ($p < .001$). Moreover, the no-psych group had scores significantly lower on this measure than the scores of the pre-psych group ($p < .001$), but the no-psych group did not differ significantly from the post-psych group. No other significant group differences were found.

On the neuroticism subscale of the NEO PI-R, significant differences were found across groups ($F[3, 130] = 18.10, p < .001$). The pre-psych and post-psych groups showed significantly greater neuroticism than did healthy controls ($p < .001$). Whereas the pre-psych group scored significantly higher on the measure of neuroticism than did the no-psych group ($p < .001$), there were no differences between the no-psych and post-psych groups on this measure. Finally, the pre-psych group had scores higher than those of both other CFS groups, reflecting the highest degree of neuroticism ($p < .001$).

Fatigue

As Table 4 indicates, there were significant group differences across the measure of fatigue ($F[3, 133] = 168.20, p < .001$). The three CFS groups did not differ from one another on this measure (all p values $> .05$), but all three groups showed greater fatigue than healthy controls (all p values $< .001$).

Neuropsychological Outcomes

As Table 5 indicates, the following differences were found on each of the measures. On the Paced Serial Addition Test, California Verbal Learning Test (trials 1 to 5; short delay, free recall; and long delay, free recall) and on the digit span (backward) and vocabulary subtests of the WAIS-R, no significant group differences were observed. On the Trail Making Test, the healthy control group and the no-psych

group were significantly quicker than the pre-psych group in completing parts A and B ($p < .05$). No other differences were found for this measure. Finally, on the digit span (forward) subtest of the WAIS-R, all three groups significantly outperformed the pre-psych group ($p < .05$), and no other differences were observed. Thus, overall, when differences in neuropsychological functioning were found to exist, the pre-psych group consistently was the most impaired.

Discussion

The findings of the current investigation suggest that psychiatric illness affects health-related quality of life in CFS. Overall, as expected, individuals with CFS and a psychiatric illness have a worse psychological well-being than individuals with CFS and no psychiatric history. Individuals with psychiatric histories that predated the onset of their CFS also had higher levels of neuroticism and greater depression and anger than did other patients with CFS. Finally, this subset of patients with CFS performed worse on some neuropsychological measures than did healthy controls and patients with CFS but no history of psychiatric illness. Reduced performance was seen on measures of attention and concentration, which are the areas of deficit most commonly seen in CFS. These data indicate that psychiatric history clearly affects quality of life in CFS and that those patients with a longstanding history of psychiatric illness are affected the most.

Despite the decreases in psychological well-being, psychiatric status did not seem to affect physical functional status adversely. In fact, there was a trend toward worse physical functioning in our group of patients with CFS but no psychiatric history ($p = .063$). This finding of worse physical functioning in patients with CFS but no psychiatric history is consistent with our earlier work (Tiersky et

al., 2000). As a possible explanation for these findings, we hypothesized (Tiersky et al., 2001) that patients with CFS and a psychiatric history had a psychiatric cause for their illness that may be expected to wax and wane over time. In contrast, we hypothesized that patients with CFS but no history of psychiatric disturbance may have a neurological basis for their illness. The findings of the current investigation lend some support to the notion that there is a subgroup of patients with CFS but no psychiatric illness and predominantly physical disability. There also appears to be a group of patients with CFS, those who have any lifetime psychiatric illness, whose illness course is strongly influenced by psychiatric factors.

We also found no evidence to support our hypothesis that having concurrent psychiatric illness would produce a double illness burden resulting in worse functional status than in ill people without comorbid psychiatric illness. Although our earlier study of veterans with CFS possibly lacked sufficient power to document the phenomenon, such is not the case in the current investigation, in which sample sizes were adequate to detect group differences. Indeed, power estimates indicated that, assuming a moderate effect size ($f = .30$) and conventional $\alpha = .05$, there was a 95% likelihood of finding significant group differences if they existed. Thus, it appears that the existence of comorbid psychiatric conditions in individuals with CFS does not produce further physical disability. One reason that the double illness burden may not be observed is the magnitude of disability produced by CFS. This "floor" effect has been documented in other studies that have investigated health-related quality of life in chronic conditions (Bindman et al., 1990).

The patients with CFS in the current investigation showed a worse health-related quality of life than did healthy controls in almost every domain. In fact, the patients with CFS generally performed at two standard deviations below the norms of controls on the SF-36 PCS subscale, indicating profound physical impairment. These scores tended to be at least one standard deviation below the published norms for patients with type II diabetes, arthritis, cancer, congestive heart failure, hypertension, and myocardial infarction (Ware et al., 1993). Performance of the CFS groups on the SF-36 MCS subscale were overall less impaired, with the two psychiatric groups performing generally one standard deviation below the healthy group. These subjects performed within the range of patients with major depression, according to published norms. Thus, this study corroborates the findings of authors who have documented that patients with CFS show significant im-

pairment on the SF-36 (Buchwald et al., 1996; Komoroff et al., 1996).

Because we found that illness duration and severity of psychiatric illness were responsible for differences in functional status among patients with CFS, these variables appear to be important stratification variables in evaluating functional well-being in CFS, especially when examining neuropsychological functioning and psychosocial well-being. That duration and severity of psychiatric illness do have some effect on neuropsychological performance and that few studies have controlled for these factors may explain the discrepant findings in the area. A future investigation should further examine the relationship between psychiatric history and neuropsychological functioning in CFS by using a more comprehensive battery to elucidate any associations more clearly.

References

- Anderson JS, Ferrans CE (1997) The quality of life in persons with chronic fatigue syndrome. *J Nerv Ment Dis* 185:359–367.
- Bindman AB, Keane D, Lurie N (1990) Measuring health changes among severely ill patients. The floor phenomenon. *Medical Care* 28:1142–1152.
- Bombardier CH, Buchwald D (1996) Chronic fatigue, chronic fatigue syndrome, and fibromyalgia disability and health care use. *Medical Care* 34(9):924–930.
- Brittain JL, La Marche JL, Reeder KP, Kenneth P (1991) Effects of age and IQ on Paced Auditory Serial Addition Task (PASAT) performance. *Clinical Neuropsychologist* 5:163–175.
- Buchwald D, Pearlman T, Umali J, Schmaling K, Katon W (1996) Functional status in patients with chronic fatigue syndrome, other fatiguing illnesses, and healthy individuals. *Am J Med* 101:364–370.
- Christodoulou C, DeLuca J, Lange G, Johnson SK, Sisto SA, Korn L, Natelson BH (1998) Relation between neuropsychological impairment and functional disability in patients with chronic fatigue syndrome. *J Neurol Neurosurg Psychiatry* 64:431–434.
- DeLis DC, Kramer JH, Kaplan E, Ober BA (1987) California Verbal Learning Test: Adult version. San Antonio: The Psychological Cooperation.
- DeLuca J, Johnson SK, Ellis SP, Natelson BH (1997) Cognitive functioning is impaired in patients with chronic fatigue syndrome devoid of psychiatric disease. *J Neurol Neurosurg Psychiatry* 62:151–155.
- DiPino RK, Kane RL (1996) Neurocognitive functioning in chronic fatigue syndrome. *Neuropsychol Rev* 6:47–60.
- Fifer SK, Mathias SD, Patrick DL, Mazonson PD, Lubeck DP, Buesching DP (1994) Untreated anxiety among adult primary care patients in a health maintenance organization. *Arch Gen Psychiatry* 51:740–750.
- Fischler B, Dendale P, Michiels V, Cluydts R, Kaufman L, De Meirleir K (1997) Physical fatigability and exercise capacity in chronic fatigue syndrome: Association with disability, somatization and psychopathology. *J Psychosom Res* 42:369–378.
- Fukuda K, Straus SE, Hickie I, Sharpe MC, Dobbins JG, Komaroff A (1994) The chronic fatigue syndrome: A comprehensive approach to its definition and study. International Chronic Fatigue Syndrome Study Group. *Ann Intern Med* 121:953–959.
- Hays RD, Wells KB, Sherbourne CD, Rogers W, Spitzer K (1995) Functioning and well-being outcomes of patients with depression compared with chronic general medical illnesses. *Arch Gen Psychiatry* 52:11–19.

- Johnson SK, DeLuca J, Natelson BH (1996) Assessing somatization disorder in the chronic fatigue syndrome. *Psychosom Med* 58:50–57.
- Katon W, Sullivan M (1990) Depression and chronic medical illness. *J Clin Psychiatry* 51:3–11.
- Katon W (1996) Editorial: The impact of major depression on chronic medical illness. *Gen Hosp Psychiatry* 18:215–219.
- Keitner GL, Ryan CE, Miller IW, Kohn R, Epstein NB (1991) 12-month outcome of patients with major depression and comorbid psychiatric or medical illness (compound depression). *Am J Psychiatry* 148:345–350.
- Komaroff AL, Fagioli LR, Doolittle TH, Gandek B, Gleit M, Guerriero RT, Kornish J, Ware NC, Ware JE Jr, Bates DW (1996) Health status in patients with chronic fatigue syndrome and in general population and disease comparison groups. *Am J Med* 101:281–290.
- Kutner MH, Nachtsheim CJ, Wasserman W, Neter J (1996) *Applied linear statistical models (Irwin series in statistics)* Chicago: Irwin.
- Lange G, DeLuca J, Maldjian JA, Lee H-J, Tiersky L, Natelson BH (1999) Brain MRI abnormalities exist in a subset of patients with chronic fatigue syndrome. *J Neurol Sci* 171:3–7.
- Levenson JL, Hamer RM, Rossiter LF (1990) Relation of psychopathology in general medical inpatients to use and cost of services. *Am J Psychiatry* 147:1498–1503.
- Manu P, Lane TJ, Matthews DA (1992) Chronic fatigue syndromes in clinical practice. *Psychother Psychosom* 58:60–8.
- Marcus S, Robins LN, Bucholz K (1990) *Quick Diagnostic Interview Schedule 3R version 1*. St. Louis: Washington University School of Medicine.
- Martinez-Aran A, Vieta E, Colom F, Reinares M, Benabarre A, Gasto C, Salamero M (2000) Cognitive dysfunctions in bipolar disorder: Evidence of neuropsychological disturbances. *Psychotherapy and Psychosomatics* 69:2–18.
- McKay AP, Tarbuck AF, Shapleske J, McKenna PJ (1995) Neuropsychological function in manic-depressive psychosis: Evidence for persistent deficits in patients with chronic, severe illness. *Br J Psychiatry* 167:51–57.
- McNair DM, Lorr M, Droppleman LF (1981) *Profile of Mood States*. San Diego: Educational and Industrial Testing Service.
- Michiels V, Cluydts R, Fischler B, Hoffman G, Le Bon O, De Meirleir (1996) Cognitive functioning in patients with chronic fatigue syndrome. *J Clin Exp Neuropsychol* 18:666–677.
- Moss-Morris R, Petrie KJ, Large RG, Kydd RR (1996) Neuropsychological deficits in chronic fatigue syndrome. *J Neurol Neurosurg Psychiatry* 60:474–477.
- Myers C, Wilks D (1999) Comparison of Euroqol EQ-5D and SF-36 in patients with chronic fatigue syndrome. *Qual Life Res* 8:9–16.
- Natelson BH, Johnson SK, DeLuca J, Sisto S, Ellis SP, Hill N, Bergen MT (1995) Reducing heterogeneity in chronic fatigue syndrome: A comparison with depression and multiple sclerosis. *Clin Infect Dis* 21:1204–1210.
- Reitan RM, Tarshes EL (1959) Differential effects of lateralized brain lesions on the Trail Making Test. *J Nerv Ment Dis* 129:257–262.
- Sherbourne CD, Wells KB, Meredith LS, Jackson CA, Camp P (1996) Comorbid anxiety disorder and the functioning and well-being of chronically ill patients of general medical providers. *Arch Gen Psychiatry* 53:889–895.
- Schweitzer R, Kelly B, Foran A, Terry D, Whiting J (1995) Quality of life in chronic fatigue syndrome. *Soc Sci Med* 41:1367–1372.
- Smets EMA, Garssen B, Bonke B, De Haes JCJM (1995) The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. *J Psychosom Res* 39:315–325.
- Smets EMA, Garssen B, Cull A, De Haes JCJM (1996) Application of the Multidimensional Fatigue Inventory (MFI-20) in cancer patients receiving radiotherapy. *Br J Cancer* 73:241–245.
- Spitzer RL, Kroenke K, Linzer M, Hahn SR, Williams JBW, deGruy FV III, Brody D, Davies M (1995) Health-related quality of life in primary care patients with mental disorders. Results from the PRIME-MD 1000 Study. *JAMA* 274:1511–1517.
- Tiersky L, DeLuca JO, Hill N, Dhar SK, Johnson SK, Lange G, Rappolt G, Natelson BH (2001) Longitudinal assessment of neuropsychological functioning, psychiatric status, functional disability and employment status in chronic fatigue syndrome (CFS). *Appl Neuropsychol* 8:41–50.
- Tiersky L, Johnson SK, Lange G, Natelson BH, DeLuca J (1997) The neuropsychology of chronic fatigue syndrome: A critical review. *J Clin Exp Neuropsychol* 19:560–586.
- Tiersky LA, Natelson BH, Ottenweller J, Lange G, Fiedler N, DeLuca J (2000) Functional status and mood in Persian Gulf Registry veterans with fatiguing illness. *Mil Psychol* 12:233–248.
- UK 700 Group (1999) Predictors of quality of life in people with severe mental illness. Study methodology with baseline analysis in the UK 700 trial. *Br J Psychiatry* 175:426–432.
- Vollmer-Conna U, Wakefield D, Lloyd A, Hickie I, Lemon J, Bird KD, Westbrook RF (1997) Cognitive deficits in patients suffering from chronic fatigue syndrome, acute infective illness or depression. *Br J Psychiatry* 171:377–381.
- Wagner-Raphael LI, Jason LA, Ferrari JR (1999) Chronic fatigue syndrome, and psychiatric disorders: Predictors of functional status in a national nursing sample. *J Occup Health Psychol* 4:63–71.
- Ware JE Jr, Snow KK, Kosinski M, Gandek B (1993) *SF-36 Health Survey. Manual and interpretation guide*. Boston: The Health Institute, New England Medical Center.
- Warner R, Huxley P (1993) Psychopathology and quality of life among mentally ill patients in the community. British and US Samples compared. *Br J Psychiatry* 163:505–509.
- Wearden A, Appleby L (1997) Cognitive performance and complaints of cognitive impairment in chronic fatigue syndrome. *Psychol Med* 27:81–90.
- Wechsler D (1981) *Wechsler Adult Intelligence Scale-Revised, manual*. New York: The Psychological Corporation.
- Wessely S, Hotopf M, Sharpe M (1998) *Chronic fatigue and its syndromes*. London: Oxford University Press.