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Differential Diagnosis of Chronic Fatigue Syndrome and Major Depressive Disorder

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The goal of this study was to identify variables that successfully differentiated patients with chronic fatigue syndrome, major depressive disorder, and controls. Fifteen participants were recruited for each of these three groups, and discriminant function analyses were conducted. Using symptom occurrence and severity data from the Fukuda et al. (1994) definitional criteria, the best predictors were postexertional malaise, unrefreshing sleep, and impaired memory–concentration. Symptom occurrence variables only correctly classified 84.4% of cases, whereas 91.1% were correctly classified when using symptom severity ratings. Finally, when using percentage of time fatigue reported, postexertional malaise severity, unrefreshing sleep severity, confusion–disorientation severity, shortness of breath severity, and self-reproach to predict group membership, 100% were classified correctly.

Key words: chronic fatigue syndrome, depression, symptomatology, diagnostic criteria

Although the etiology of chronic fatigue syndrome (CFS) remains unknown, researchers have been able to examine and better understand the nature of this illness primarily through the use of clinical classification approaches (Jason, Fennell, & Taylor, 2003). It is important to note that neither the original U.S. case definition (Holmes et al., 1988) nor the revised U.S. case definitions for CFS (Fukuda et al., 1994) were derived empirically (Jason et al., 1997). Consequently, some CFS researchers have been concerned about which symptoms have been included within the case definition. One approach to improving the diagnostic criteria for CFS is through the development of empirically derived symptom criteria. In a study conducted by Komaroff et al. (1996), patients meeting the major criteria of both the original CFS case definition (Holmes et al., 1988) and the revised CFS case definition (Fukuda et al., 1994) were compared to healthy controls, patients with multiple sclerosis, and patients with depression. Their study found support for many of the symptoms that are included in the CFS case definitions. Hartz, Kuhn, and Levine (1998) also examined people with CFS and compared them to people with idiopathic fatigue and people with no symptoms of fatigue. Similar to Komaroff et al., Hartz et al. found support for many of the symptoms included in the current CFS case definition.

Other approaches have used artificial neural networks to classify the symptoms of patients with CFS (Linder, Dinser, Wagner, Krueger, & Hoffmann, 2002). Still other investigators have used factor analysis to better understand characteristics of those with this syndrome (Nisenbaum, Reyes, Mawle, & Reeves, 1998). Nisenbaum, Reyes, Unger, and Reeves (2004) found three factors (i.e., musculoskeletal, infection, and cognition-mood-sleep) among a sample of 1,391 chronically fatigued participants. Friedberg, Dechene, McKenzie, and Fontanetta (2000) also found three factors (cognitive problems, flu-like symptoms, and neurological symptoms) in a sample of patients with CFS. Another factor analytic study by Jason et al. (2002) found support for the existence of four distinct components of chronic fatigue: lack of energy (fatigue intensity), physical exertion (fatigue exacerbated by physical exertion), cognitive problems (difficulties with short-term memory, concentration, and information processing), and fatigue and rest (rest or sleep is not restorative). Results of the study were of theoretical importance because two of the primary dimensions of fatigue that emerged within the CFS-like group—postexertional fatigue and cognitive problems—corresponded closely with several definitional criteria for CFS (Carruthers et al., 2003; Lloyd, Hickie, Boughton, Spencer, & Wakefield, 1990).

Several investigators have argued that the CFS criteria might be improved with the inclusion of symptom

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severity ratings (Jason, King, Taylor, & Kennedy, 2000). At present, the symptom criteria for the case definition are scored as either being present or absent with no consideration given to the symptom severity. Research has suggested that this scoring system is problematic because many of the symptoms included in the diagnostic criteria for CFS are commonly experienced by people at one time or another (Deneche et al., 1996). Employing severity ratings might be particularly useful for differentiating those who have CFS from those who solely have depressive disorders. Making these diagnostic distinctions have been some of the most difficult for clinicians and researchers (Jason et al., 2003).

Jason et al. (2003) found when comparing the symptomatic criteria of participants with CFS to participants with melancholic depression, only one significant difference emerged between the groups. In other words, the occurrence of Fukuda et al.'s (1994) symptomatic criteria was very similar for the two groups. However, when symptom severity ratings were used—with a requirement for symptom severity ratings of 40 or higher as a scoring rule for determining whether the symptom fulfilled the diagnostic criteria—four significant differences emerged between the two groups. In another study, King and Jason (2005) compared three groups—CFS, major depressive disorder (MDD), and controls—and when looking at symptom occurrence alone, the CFS and MDD groups were relatively similar. Some individuals in the MDD group met the inclusionary criteria for the current U.S. case definition for CFS (i.e., the presence of fatigue plus at least four of the eight diagnostic symptoms). However, when examining differences in symptom severity ratings for fatigue and the eight symptoms of the U.S. case definition among individuals with CFS, MDD, and healthy controls, an improved ability to distinguish the CFS group from the MDD group was demonstrated. Clearly, some individuals might have both CFS and a depressive disorder, but in these studies individuals that were selected for the depression group did not have CFS.

In addition to including severity ratings, it is possible that there are other symptoms that might help better differentiate those with CFS from MDD. King and Jason (2005) also examined definitional criteria symptoms that were not included in Fukuda et al.'s (1994) study. These symptoms were from a physical, cognitive, and emotional checklist. A group of these non-Fukuda et al. definitional symptoms were identified that successfully differentiated the CFS groups from the MDD and controls (e.g., muscle weakness, need to nap each day, frequently losing train of thought, difficulty finding the right word, confusion–disorientation, hot and cold spells, feeling chilled–shivery, night sweats, shortness of breath, and blurred vision). In addition, they found that self-reported measures of activity (e.g., percentage of time performing low intensity activity, percentage of time fatigue reported) also significantly differentiated those with CFS and MDD (Hawk, Jason, & Peña, 2005). These studies suggested that there might be other critical symptoms that are not within the Fukuda et al. CFS symptom list that could be used to differentiate those with CFS and MDD.

In an effort to identify an objective method for discriminating CFS from major depression, Johnson, DeLuca, and Natelson (1995) administered the Beck Depression Inventory (BDI) to people with CFS and people with major depression. Significant differences were found in the nature of the symptoms endorsed on the BDI by people with CFS and people with major depression. The BDI scores of people with CFS comprised mainly items concerning physical complaints and somatic symptoms of fatigue. Symptoms of disturbed mood and self-reproach, two cardinal signs of depression, were not reported as frequently by the participants with CFS (Johnson et al., 1995). These findings demonstrated that although depressive symptoms are common in samples of people with CFS and depression, the types of items involved are qualitatively different. The results of this study suggested that incorporating a standardized measure, such as the BDI, into the diagnostic procedure for CFS may help clinicians distinguish cases of CFS from cases of major depression.

The assessment and diagnosis of CFS is a difficult process that is complicated by the overlap of symptoms with many other disorders, and this is particularly true for the depressive disorders. Without clear diagnostic markers, case identification for CFS and the differentiation from other disorders depends on information obtained through clinical interviews (Fukuda et al., 1994). Our study sought to investigate whether additional measures of functioning and symptomatology identified in two previous investigations (Hawk et al., 2005; King & Jason, 2005) could be used to improve efforts to distinguish cases of CFS from depression and healthy controls. In addition, it was hypothesized that severity ratings, as opposed to occurrence ratings, would be more successful in differentiating individuals with CFS from those with depression or controls.

Method

Participants

A total of 45 individuals (15 with CFS, 15 with MDD, and 15 healthy controls) were recruited from the greater Chicago area for this study. Fifteen participants with CFS were solicited to participate. Participants were drawn from two sources: a local CFS support group in Chicago and previous research studies con-

ducted at DePaul University. Participants were required to have been diagnosed with CFS, using Fukuda et al.'s (1994) diagnostic criteria, by a board-certified physician and were required to have a current (active) case of CFS. All participants had been seen by their physician in the past year. Individuals who reported having uncontrolled or untreated medical illnesses (e.g., untreated anemia) were excluded. All participants were screened with the Structured Clinical Interview for the DSM–IV (SCID–IV; to be described later) to ensure that they did not have any exclusionary psychiatric illnesses as stipulated by the Fukuda et al. case definition.

Fifteen participants with a diagnosis of MDD were solicited from a local chapter of the National Depressive and Manic Depressive support group in Chicago. Participants were required to have been diagnosed with major depression by a licensed psychologist or psychiatrist. All participants were screened with the SCID–IV to ensure that they met criteria for a current (active) case of major depression and did not have any other current psychiatric illnesses. Individuals who had other current psychiatric conditions, in addition to major depression, were excluded. Individuals who reported having uncontrolled or untreated medical illnesses (e.g., anemia, diabetes) were also excluded.

Finally, 15 healthy control participants were solicited from the greater Chicago area. Individuals who did not have any medical illnesses or who did not have any uncontrolled or untreated illnesses (e.g., anemia, diabetes) were allowed to participate. All participants were screened with the SCID–IV to ensure that they did not have any current psychiatric illnesses. Individuals with current psychiatric conditions were excluded.

Procedure

All 45 participants were initially screened by a trained interviewer to determine if they met the inclusion and exclusion criteria of the group condition for which they were being considered (i.e., CFS, MDD, or healthy control). As part of this screening process, all participants were administered the SCID–IV to assess psychiatric conditions. Participants who met criteria for participation were asked to complete a battery of questionnaires that measure demographics; social, emotional, and physical functioning; activity level; depression; and a comprehensive list of physical, cognitive, and emotional symptoms.

Measures

Demographic variables. Basic demographic data were gathered, including age, ethnicity, marital status, gender, occupation, work status, and educational level. Socioeconomic status was measured using occupation and highest educational level to compute the revised Hollingshead scale (Wasser, 1991) of socioeconomic status.

Physical, cognitive, and emotional symptom checklist. Participants were asked to provide data for fatigue and the eight diagnostic symptoms specified by the Fukuda et al. (1994) case definition. They were asked to report if each symptom had been present for 6 months or longer, began before the onset of their fatigue or health problems, how often it is experienced, and rate the intensity of each symptom on the same 101-point scale ranging from 0 (*XXX*) to 100 (*XXX*).

Participants were asked to indicate whether they had a number of somatic, cognitive, and emotional symptoms commonly experienced by people with CFS. Symptoms on this list were taken from a variety of sources, including a measure developed by Komaroff et al. (1996), the current U.S. CFS case definition (Fukuda et al., 1994), and the results of studies by Hartz et al. (1998) and Komaroff et al. (1996) that suggested the inclusion of new symptoms in the case definition. For each symptom, participants were asked to indicate if the symptom had been present for 6 months or longer, if the symptom began before the onset of their fatigue or health problems, and how often the symptom is experienced. Participants were also asked to rate the intensity of each symptom they endorsed on a 101-point scale ranging from 0 (*no problem*) to 100 (*the worst problem possible*).

A prior study by King and Jason (2005) found that the CFS group compared to the MDD group and control group had significant differences for the following items rated on severity: four symptoms in the fatigue–weakness group (fatigue, postexertional malaise, muscle weakness, and need to nap each day), three symptoms in the neuropsychological category (frequently losing train of thought, difficulty finding the right word, and confusion–disorientation), four symptoms in the infectious category (sore throat, tender lymph nodes, hot and cold spells, and feeling chilled–shivery), three symptoms in the rheumatological category (muscle pain, pain in multiple joints without swelling, and night sweats), one symptom in the cardiopulmonary (shortness of breath), and one symptom in the neurological category (blurred vision) and unrefreshing sleep. Therefore, these items were used in our study.

BDI. This is a self-rating scale that evaluates 21 symptoms related to depression on a 4-point scale ranging from 0 (*absent*) to 3 (*most severe*). Internal consistency for the BDI ranges from .73 to .92 with a mean of .86. (Beck, Steer, & Garbin, 1988). The BDI demonstrates high internal consistency, with alpha coefficients of .86 and .81 for psychiatric and non-psychiatric populations, respectively (Beck et al., 1988).

The BDI has a split-half reliability coefficient of .93 (Beck et al., 1988). Research has shown that the individual questions on the BDI can be divided into four categories: mood, self-reproach, somatic, and vegetative characteristics of depression (Huber, Freidenberg, Paulson, Shuttleworth, & Christy, 1990; Huber, Rammonhan, Bornstein, & Christy, 1993). A prior study found the self-reproach items significantly differentiated those with CFS from those with MDD and controls (King & Jason, 2005).

Activity Record (ACTRE). The ACTRE is a daily self-administered log of physical activity. Respondents log their daily activities per every ½ hr over the course of 2 days. Respondents rate the intensity of their activity (e.g., sedentary or active) and classify the nature of their activity into one of the nine following categories for every recorded ½ hr of activity: sleep (going to bed for the night), household activities (cleaning, mending, shopping for or putting away groceries, gardening, or similar activities), work (paid or volunteer activities in or out of the home, schoolwork, writing papers, attending classes, studying, or similar activities), self-care (personal care activities including dressing, grooming, exercises, normal meals, showering, or similar activities), recreation or leisure (hobbies, television, games, reading, sports, going out for meals, movies, shopping, talking with friends, or similar activities), rest (rest periods ½ hr or longer), preparation or planning (time spent preparing to do an activity or planning daily or weekly activities), transportation (traveling to and from activities), and treatment (doctor or therapy appointments and home - exercises).

Respondents also answer eight questions for every ½ hr of recorded activity that assess whether the activity is associated with pain or fatigue, and whether each activity is perceived as difficult to perform, meaningful, enjoyable, or well done. Need for rest is also assessed every ½ hr. Data collected on the ACTRE can be totaled and specific abilities can be rated in terms of associated symptoms. In effect, clinicians are able to obtain a composite that represents a comprehensive profile of functioning as well as areas of dysfunction (Gerber & Furst, 1992). In a validation study of the ACTRE, Gerber and Furst demonstrated that the ACTRE has adequate psychometric properties as a measure of activity and functional status in a population with a chronic disabling condition. A prior study by Hawk et al. (2005) found that the following variables best discriminated those with CFS from MDD and controls: percentage of time performing low intensity activity, percentage of time fatigue was reported, percentage of time activity produced fatigue, percentage of time rest during activity was needed, and percentage of time in rest periods.

The SCID. The SCID is a valid and reliable semistructured interview guide that closely resembles a traditional psychiatric interview (Spitzer, Williams, Gibbon, & First, 1995). The SCID is designed to identify current, past, and lifetime (chronic or reoccurring, current and past) diagnoses for a majority of DSM–IV, Axis I psychiatric disorders. The SCID is commonly administered during a single session lasting 45 min to 1 hr. Diagnostic decisions generated by the SCID are based on all possible sources of historical, symptomatic, and behavioral information. The SCID begins with a semistructured interview portion designed to yield a tentative diagnosis. The tentative diagnosis is then systematically assessed during the structured portion of the interview through the use of embedded questions that conform to the exact, Axis I criteria set forth by the DSM–IV.

Statistical Approach

One stepwise discriminant function analyses was performed using the occurrence data for the eight Fukuda et al. (1994) case definition symptoms as predictors of group membership (CFS, MDD, and controls). A second stepwise discriminant function analysis used the severity data for the eight Fukuda et al. case definition symptoms as predictors. The final discriminant function analysis used a wider set of Fukuda et al. variables and other variables as predictors.[1]

There were no missing data. One variable used in the analyses did not have a normal distribution. The distribution of the variable "night sweats" had a moderate departure from normality. The analyses were performed on the raw data and then repeated after a square root transformation was used to correct the distribution of this variable. Results between the raw data and the transformed data were compared, and no major differences were noted (i.e., variables in the equation and classification were the same). Because no differences in outcomes were observed, the raw data were used in the analyses.

Results

Sociodemographic data were compared across the three groups using Pearson's chi-square for dichotomous and multinomial data and analysis of variance for age and socioeconomic status. There were no signifi-

[1]When there are three groups, two discriminant functions can be calculated, and the first function has the largest ratio of between-groups to within-groups sums of squares, and the second function has the next largest ratio (this second function is uncorrelated with the first). In other words, the two discriminant functions are uncorrelated with each other and maximize the ratio of between-groups to within-groups sums of squares.

cant differences between groups with respect to gender, race, age, socioeconomic status, education, marital status, occupation, work status, and additional roles (see King & Jason, 2005).

In regard to psychiatric comorbidity, 3 participants (20%) in the CFS group met DSM–IV diagnostic criteria for dysthymia. No other current diagnoses were detected in the CFS group. In the MDD group, all 15 participants (100%) met DSM–IV diagnostic criteria for MDD. None of the participants in the MDD group met criteria for MDD with catatonic, melancholic, psychotic, or atypical features. Participants in the MDD group did not meet criteria for any other Axis I disorders. None of the participants in the control group met criteria for any Axis I disorder.

Discriminant Function Analyses

The first stepwise discriminant function analysis was performed using the occurrence data for the eight Fukuda et al. (1994) case definition symptoms as predictors of group membership (CFS, MDD, and controls). Results of the stepwise analysis reveal that three of the eight predictor variables—postexertional malaise, unrefreshing sleep, and impaired memory–concentration—were good discriminators among the three groups. Two discriminant functions were calculated with a combined, $\chi^2(6, N = XX) = 89.14$, $p < .01$. After removal of the first function,[2] there was still a strong association between groups and predictors, $\chi^2(2, N = XX) = 27.23$, $p < .01$. The two discriminant functions accounted for 78.9% and 21.1%, respectively, of the between-groups variability. The loading matrix of correlations between predictors and discriminant functions suggests that the best predictors for distinguishing between CFS, MDD, and control participants were postexertional malaise and unrefreshing sleep. Participants with CFS experienced more postexertional malaise (100%) than MDD (20%) and control participants (6%). Likewise, participants with CFS experienced more unrefreshing sleep (100%) than MDD (93%) and control participants (20%). For impaired memory–concentration, participants with CFS experienced more problems with impaired memory–concentration (93%) than MDD (87%) and control participants (20%). Using postexertional malaise, unrefreshing sleep, and impaired memory–concentration as predictors of group membership, 38 cases (84.4%) were correctly classified. The 7 errors in classification were as follows: 3 depression participants misclassified in the CFS group, 1 depression participant misclassified as a control, 2 controls misclassified in the depression group, and 1 control misclassified in the CFS group.

A second stepwise discriminant function analysis was performed using the severity data for the eight symptoms of the U.S. case definition as predictors of group membership (CFS, MDD, and controls). Results of the stepwise analysis reveal that three of the eight predictor variables—postexertional malaise, unrefreshing sleep, and impaired memory–concentration—were good discriminators among the three groups. Two discriminant functions were calculated with a combined, $\chi^2(6, N = XX) = 92.78$, $p < .01$. After removal of the first function, there was still a strong association between groups and predictors, $\chi^2(2, N = XX) = 22.82$, $p < .01$. The two discriminant functions accounted for 85.8% and 14.2%, respectively, of the between-groups variability. The loading matrix of correlations between predictors and discriminant functions suggests that the best predictors for distinguishing between CFS, MDD, and control participants were postexertional malaise severity and unrefreshing sleep severity. Participants with CFS had more severe postexertional malaise (M = 73.33) than MDD (M = 8.67) and control participants (M = 4.67). Likewise, participants with CFS had more severe unrefreshing sleep (M = 75.60) than MDD (M = 44.33) and control participants (M = 5.33). With respect to impaired memory–concentration, participants with CFS had more severe impaired memory–concentration (M = 61.67) than MDD (M = 41.33) and control participants (M = 7.00). Using severity ratings for postexertional malaise, unrefreshing sleep, and impaired memory–concentration as predictors of group membership, 41 cases (91.1%) were correctly classified. The 4 errors in classification were as follows: 1 CFS participant was misclassified in the MDD group, 1 MDD participant was classified in the CFS group, and 2 MDD participants were misclassified as controls.

A third stepwise discriminant function analysis was performed using variables identified in earlier analyses (see Hawk et al., 2005; King & Jason, 2005). Results of the stepwise analysis indicate that only 6 of the 24 predictor variables were selected for inclusion: percentage of time fatigue was reported, postexertional malaise severity, unrefreshing sleep severity, confusion–disorientation severity, shortness of breath severity, and self-reproach (see Table 1). Two discriminant functions were calculated with a combined, $\chi^2(12, N = XX) = 142.71$, $p < .01$. After removal of the first function, there was still a strong association between groups and predictors, $\chi^2(5, N = XX) = 46.60$, $p < .01$. The two discriminant functions accounted for 82.2% and 17.8%, respectively, of the between-groups variability. The loading matrix of correlations between predictors and discriminant functions suggests that the best predictors for distinguishing between CFS, MDD, and control participants were percentage of time fatigue

[2]When there are several groups, as in the case in our study, a case's values on all functions must be considered simultaneously. In addition, when there is more than one function, it is possible to test the means of the functions by first testing all means simultaneously and then excluding one function at a time, testing the means of the remaining functions at each step.

Table 1. *Predictor Variables in Stepwise Discriminant Function Analysis Using 24 Additional Symptoms*

Step	Predictor Variable	Variables in Discriminant Function	Wilks's λ	Equivalent *F*(2, 42)
1	Percentage of time fatigue reported	1	.22	72.63*
2	Self-reproach	2	.12	39.15*
3	Postexertional malaise	3	.07	36.87*
4	Confusion	4	.05	34.57*
5	Shortness of breath	5	.03	33.86*
6	Unrefreshing sleep	6	.03	31.38*

*$p < .01$.

Table 2. *Correlations Between Discriminating Variables and Discriminant Functions (Function Structure Matrix) and Standardized Discriminant Function Coefficients for Additional Symptoms*

	Correlation With Discriminant Functions		Standardized Discriminant Function Coefficients	
Predictor Variable	Function 1	Function 2	Function 1	Function 2
Percentage of time fatigue reported	.57	.12	.96	.28
Self-reproach	.11	.65	–.19	.92
Postexertional malaise	.52	–.36	.51	–.53
Confusion	.19	–.09	.39	–.81
Shortness of breath	.15	–.12	–.85	–.09
Unrefreshing sleep	.11	.65	.53	.40

was reported, postexertional malaise severity, unrefreshing sleep severity, and self-reproach (see Table 2). Participants with CFS experienced fatigue ($M = 75.14$) more often than depressed ($M = 35.89$) or control participants ($M = 4.34$). Participants with CFS also had more severe postexertional malaise ($M = 73.33$) than MDD ($M = 8.67$) and control participants ($M = 4.67$). Likewise, participants with CFS had more severe unrefreshing sleep ($M = 75.60$) than MDD ($M = 44.33$) and control participants ($M = 5.33$). Using percentage of time fatigue was reported, postexertional malaise severity, unrefreshing sleep severity, confusion–disorientation severity, shortness of breath severity, and self-reproach to predict group membership, 45 participants (100%) were classified correctly.

Discussion

In the first stepwise discriminant function analysis, symptom occurrence data for the eight symptoms of the U.S. diagnostic criteria for CFS reveal that postexertional malaise, unrefreshing sleep, and impaired memory–concentration were the best predictors (i.e., 84.4% correct classification). A second discriminant function analyses was performed using severity ratings for the eight symptoms of the current CFS diagnostic criteria, and results reveal that once again, postexertional malaise, unrefreshing sleep, and impaired memory–concentration were the best predictors of group membership. In this analysis, there was a 91.1% correct classification. These findings indicate that the use of severity ratings for the eight symptoms of the CFS diagnostic criteria led to fewer misclassifications. A final stepwise discriminant function analysis was performed in which 6 of the 24 variables were found to be the best predictors of group membership: percentage of time fatigue was experienced, self-reproach, postexertional malaise, unrefreshing sleep, confusion–disorientation, and shortness of breath. Using these 6 predictors, 100% of the study participants were correctly classified.

In the first two stepwise discriminant function analyses using symptom occurrence data and severity data, postexertional malaise, memory–concentration difficulties, and unrefreshing sleep were the only variables kept in the analyses. This suggests these variables are good discriminators of CFS, MDD, and controls. Exercise intolerance, sleep difficulties, and cognitive difficulties have been repeatedly demonstrated to be prominent features of CFS (Jason, Taylor, et al., 2001; Jason & Taylor, 2002). In the final stepwise discriminant function analysis, fatigue, postexertional malaise, unrefreshing sleep, and confusion–disorientation were 4 of the 6 variables kept in the equation out of a total of 24 predictor variables initially entered. These findings are also consistent with those of Jason, Taylor, et al. Taken together, the findings of Jason, Taylor, et al. and the results of our study suggest that fatigue, unrefreshing sleep, postexertional malaise, and cognitive functioning represent important markers in the assessment of CFS.

The best results in classification were achieved when a wide variety of measures was used and new

symptoms found to distinguish cases of CFS from MDD and controls were included. For example, the inclusion of self-reproach in the final equation was not surprising in light of the findings of Johnson et al. (1996). Self-reproach appears to be a crucial variable for discriminating between people who have CFS and MDD. As noted before, self-reproach is much less commonly present in people with CFS when compared to people with MDD.

The inclusion of shortness of breath in the final equation is of interest as well because this symptom is not currently included in the Fukuda et al. (1994) case definition. A study by Jason, Torres-Harding, Carrico, and Taylor (2001) with a different sample also found shortness of breath to be a good discriminator among CFS, melancholic depression, and healthy controls. Jason, Torres-Harding, et al. suggested that this finding may be indicative of neurally mediated hypotension in people with CFS. Neurally mediated hypotension is defined as a 30-mm Hg drop in systolic, or a 15-mm Hg drop in diastolic, blood pressure occurring in response to an orthostatic challenge (e.g., standing upright after sitting or laying down; Rowe & Calkins, 1998).

Included within the predictors entered into the final stepwise analysis were two measures of fatigue: One was a simple severity rating of fatigue on a 101-point scale ranging from 0 (*XXX*) to 100 (*XXX*), and the other was the percentage of time fatigue was reported on the ACTRE. Results of the analysis reveal that only one of these measures was a good predictor of group membership: percentage of time fatigue was reported on the ACTRE. This may suggest that fatigue is best measured by a daily log over a 2-day period of time versus a one-item severity rating score. Assessing fatigue over the span of 2 days may be more valid than assessment at one point in time because fatigue levels are variable for many people. Furthermore, the fluctuating nature of fatigue and the other symptoms of CFS are a commonly reported feature of this illness. Finally, as Stouten (2005) correctly mentioned, many frequently used fatigue scales do not accurately represent the severe fatigue that is characteristics of CFS (although this problem is avoided with the Profile of Fatigue-Related Symptoms; Ray, Weir, Phillips, & Cullen, 1992).

There are several limitations in this study. The sample sizes were relatively small; thus, the study needs to be replicated with larger samples. With such a small sample, there are methodological problems that are encountered, particularly when multiple predictor variables are employed. In addition, the use of stepwise discriminant function analysis can be problematic in general because it capitalizes on chance for the order of variable inclusion. Also, data may be over-fitted because the equation derived from a single sample is too close to the sample and may not generalize to the population.

CFS is a difficult condition to diagnose, because the signs and symptoms of this illness overlap with other medical and psychiatric condition (Taylor, Jason, & Schoeny, 2001). Several key symptoms and their severity ratings may assist the accurate diagnosis of CFS and differentiate it from MDD. The current definitional symptoms of postexertional malaise, unrefreshing sleep, and impaired memory–concentration appear to be particularly important in distinguishing CFS from MDD. In addition, self-reproach items on the BDI appear useful to indicate the presence of MDD rather than CFS. Finally, using symptoms that are not currently part of the CFS case definition, such as activity levels and shortness of breath, and measuring fatigue over the course of 2 days, might also increase the ability to differentiate people with CFS from those with solely depressive disorders.

References

Beck, A. T., Steer, R. A., & Garbin, M. G. (1988). Psychometric properties of the Beck Depression Inventory: Twenty-five years of evaluation. *Clinical Psychology Review, 8*(1), 77–100.

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. *The American Journal of Medicine, 101*(4), 364–370.

Carruthers, B. M., Jain, A. K., DeMeirleir, K. L., Peterson, D. L., Klimas, N. G., Lerner, A. M., et al. (2003). Myalgic encephalomyelitis/chronic fatigue syndrome: Clinical working case definition, diagnostic and treatments protocols. *Journal of Chronic Fatigue Syndrome, 11,* 7–115.

Dowsett, E. G., Goudsmit, E., Macintyre, A., & Shepherd, C. (1994). *London criteria for M.E.* Report from The National Task Force on chronic fatigue syndrome (CFS), post viral fatigue syndrome (PVFS), myalgic encephalomyelitis (ME). Bristol, England: Westcare.

Friedberg, F., Dechene, L., McKenzie, M. J., II, & Fontanetta, R. (2000). *Journal of Psychosomatic Research, 48*(1), 59–68.

Fukuda, K., Straus, S. E., Hickie, I., Sharpe, M. C., Dobbins, J. G., & Komaroff, A. (1994). The chronic fatigue syndrome: A comprehensive approach to its definition and study. *Annals of Internal Medicine, 121,* 953–959.

Gerber, L., & Furst, G. (1992). Validation of the NIH Activity Record: A quantitative measure of life activities. *Arthritis Care and Research, 5,* 81–86.

Hartz, A., Kuhn, E. M., & Levine, P. H. (1998). Characteristics of fatigued persons associated with features of chronic fatigue syndrome. *Journal of Chronic Fatigue Syndrome, 4,* 71–97.

Hawk, C., Jason, L. A., & Peña, J. (2005). *ACTRE variables that differentiate chronic fatigue syndrome from depression.* Manuscript submitted for publication.

Holmes, G. P., Kaplan, J. E., Gantz, N. M., Komaroff, A. L., Schonberger, L. B., Strauss, S. S., et al. (1988). Chronic fatigue syndrome: A working case definition. *Annals of Internal Medicine, 108,* 387–389.

Huber, S., Freidenberg, D., Paulson, G., Shuttleworth, E., & Christy, J. (1990). The pattern of depressive symptoms varies with progression of Parkinson's disease. *Journal of Neurology, Neurosurgery & Psychiatry, 53,* 275–278.

Huber, S., Rammonhan, K., Bornstein, R., & Christy, J. (1993). Depressive symptoms are not influenced by severity of multiple

sclerosis. *Neuropsychology, Neuropsychiatry, and Behavioral Neurology, 6,* 177–180.

Jason, L. A., Fennell, P., & Taylor, R. R. (Eds.). (2003). *Handbook of chronic fatigue syndrome.* New York: Wiley.

Jason, L. A., King, C. P., Taylor, R. R., & Kennedy, C. (2000). Defining chronic fatigue syndrome: Methodological challenges. *Journal of Chronic Fatigue Syndrome, 7*(3), 17–32.

Jason, L. A., Richman, J. A., Friedberg, F., Wagner, L., Taylor, R., & Jordan, K. M. (1997). Politics, science, and the emergence of a new disease: The case of chronic fatigue syndrome. *American Psychologist, 52,* 973–983.

Jason, L. A., & Taylor, R. R. (2002). Applying cluster analysis to define a typology of chronic fatigue syndrome in a medically-evaluated, random community sample. *Psychology and Health, 17,* 323–337.

Jason, L. A., Taylor, R. R., Kennedy, C. L., Harding, S. T., Song, S., Johnson, D., et al. (2001). Subtypes of chronic fatigue syndrome: A review of findings. *Journal of Chronic Fatigue Syndrome, 8,* 1–21.

Jason, L. A., Taylor, R. R., Kennedy, C. L., Jordan, K., Huang, C., Torres-Harding, S., et al. (2002). A factor analysis of chronic fatigue symptoms in a community-based sample. *Social Psychiatry and Psychiatric Epidemiology, 37,* 183–189.

Jason, L. A., Torres-Harding, S. R., Taylor, R. R., & Carrico, A. W. (2001). A comparison of the 1988 and 1994 diagnostic criteria for chronic fatigue syndrome. *Journal of Clinical Psychology in Medical Settings, 8,* 337–343.

Johnson, S. K., DeLuca, J., & Natelson, B. (1995). Depression in fatiguing illness: Comparing patients with chronic fatigue syndrome, multiple sclerosis and depression. *Journal of Affective Disorders, 39,* 21–30.

King, C., & Jason, L. A. (2005). Improving the diagnostic criteria and procedures for chronic fatigue syndrome. *Biological Psychology, 68,* 87–106.

Komaroff, A. L., Fagioli, L. R., Geiger, A. M., Doolittle, T. H., Lee, J., Kornish, R. J., et al. (1996). An examination of the working case definition of chronic fatigue syndrome. *The American Journal of Medicine, 100,* 56–64.

Linder, R., Dinser, R., Wagner, M., Krueger, G. R., & Hoffmann, A. (2002). Generation of classification criteria for chronic fatigue syndrome using an artificial neural network and traditional criteria set. *In Vivo, 16*(1), 37–43.

Lloyd, A. R., Hickie, I., Boughton, C. R., Spencer, O., & Wakefield, D. (1990). Prevalence of chronic fatigue syndrome in an Australian population. *Medical Journal of Australia, 153,* 522–528.

Nisenbaum, R., Reyes, M., Mawle, A. C., & Reeves, W. C. (1998). Factor analysis of unexplained severe fatigue and interrelated symptoms: Overlap with criteria for chronic fatigue syndrome. *American Journal of Epidemiology, 148,* 72–77.

Nisenbaum, R., Reyes, M., Unger, E. R., & Reeves, W. C. (2004). Factor analysis of symptoms among subjects with unexplained chronic fatigue: What can we learn about chronic fatigue syndrome? *Journal of Psychosomatic Research, 56*(2), 171–8.

Ray, C., Weir, W. R. C., Phillips, S., & Cullen, S. (1992). Development of a measure of symptoms in chronic fatigue syndrome: The profile of fatigue-related symptoms (PFRS). *Psychology and Health, 7,* 27–43.

Spitzer, R. L., Williams, J. B. W., Gibbon, M., & First, M. B. (1995). *Structured clinical interview for the DSM-IV: Non-Patient Edition (SCID: NP, Version 2.0).* Washington, DC: American Psychiatric Press.

Stewart, A. L., Greenfield, S., Hays, R. D., Wells, K., Rogers, W. H., Berry, D., et al. (1989). Functional status and well-being of patients with chronic conditions: Results from the Medical Outcomes Study. *The Journal of the American Medical Association, 262*(7), 907–13.

Stouten, B. (2005). *Identification of ambiguities in the 1994 chronic fatigue syndrome research case definition and recommendations for resolution.* BMC Health Services Research 2005, 5:37 doi:10.1186/1472–6963–5–37.

Taylor, R. R., Jason, L. A., & Schoeny, M. E. (2001). Evaluating latent variable models of functional somatic distress in a community-based sample. *Journal of Mental Health, 10,* 335–349.

Ware, J. E., Jr., & Sherbourne, C. D. (1992). The MOS 36-item short-form health survey (SF-36): Conceptual framework and item selection. *Medical Care, 30*(6), 473–83.