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Chronic Fatigue Syndrome Versus Sudden Onset Myalgic Encephalomyelitis

Leonard A. Jason,
DePaul University

Meredyth Evans,
DePaul University

Abigail Brown,
DePaul University

Madison Sunnquist, and
DePaul University

Julia L. Newton
Newcastle University

Abstract

A revised sudden onset case definition for Myalgic Encephalomyelitis (ME) has been developed (Jason, Damrongvachiraphan, Hunnell, Bartgis, Brown, Evans, & Brown, 2012) based on past case definitions. In a prior study, Jason, Brown, Clyne, Bartgis, Evans, and Brown (2012) compared patients recruited using the 1994 case definition of chronic fatigue syndrome (CFS) to contrast those meeting criteria for the revised ME criteria. They found that this revised ME case definition identified patients with more functional impairments and physical, mental, and cognitive problems than those meeting the CFS criteria. The study by Jason, Brown, et al. (2012) only selected individuals who first met the CFS criteria, and it only relied on one Chicago based data set. The current study replicated this comparison with two distinct data sets with different case ascertainment methods. Results indicate that the ME criteria identified a group of patients with more functional disabilities as well as more severe post-exertional malaise symptoms.

The illness known as Myalgic Encephalomyelitis (ME) was first described in literature of the 1930s, where an outbreak of Epidemic Neuromyasthenia in L.A. County was called “atypical poliomyelitis” because of its resemblance to polio (Gilliam, 1938; Hyde, 2007). Then, an anonymous editorial of a 1956 issue of the *Lancet* coined the term benign Myalgic Encephalomyelitis (Anonymous Editorial, 1956). It was called ‘benign’ because the illness did not lead to patient death. Later, Ramsay (1988) published a definition of this disease using the term Myalgic Encephalomyelitis (ME) and the term benign was dropped due to the seriousness of the disability created by the illness (Hyde, Goldstein, & Levine, 1992). Others have also contributed to the specification of ME over the last few decades (Carruthers, van

de Sande, De Meirleir, Klimas, Broderick, Mitchell, et al., 2011; Dowsett, Goudsmit, Macintyre, & Shepherd, 1994; Dowsett, Ramsay, McCartney, & Bell, 1990; Goudsmit, Shepherd, Dancey, & Howes, 2009). Unfortunately, problems have occurred in replicating findings, particularly in the search for biological markers, and this might be due to the heterogeneous patient samples that are a result of case definition ambiguities (Jason, Helgersen, Torres-Harding, Carrico & Taylor, 2003).

In the mid-1990s, an international working group developed a case definition for chronic fatigue syndrome (CFS) (Fukuda et al., 1994), which required a person to experience six or more months of chronic fatigue of a new or definite onset, that is not substantially alleviated by rest, not the result of ongoing exertion, and results in substantial reductions in occupational, social, and personal activities. The Fukuda et al. (1994) case definition uses a set of symptoms in which not all need to be present to make a diagnosis. For example, because the Fukuda et al. (1994) criteria only require four symptoms out of a possible eight, critical CFS symptoms such as post-exertional malaise and memory and concentration problems are not required of all patients. This CFS case definition has been criticized for lacking operational definitions and guidelines to assist health care professionals in their application of these criteria (Jason et al., 1999; Reeves et al., 2003).

When Jason, Helgersen, Torres-Harding, Carrico, and Taylor (2003) attempted to operationalize the ME criteria by selecting individuals with post-exertional malaise, memory and concentration impairment, and fluctuation of symptoms, and then compared these patients to those meeting the current US definition of CFS (Fukuda et al., 1994), the ME criteria selected a more symptomatic group of patients. Several years later, Jason, Damrongvachiraphan, et al. (2012) attempted to better operationalize the ME criteria, based on the work of a number of theorists and practitioners (Dowsett, Goudsmit, Macintyre, & Shepherd, 1994; Dowsett, Ramsay, McCartney, & Bell, 1990; Goudsmit, Shepherd, Dancey, & Howes, 2009; Hyde, Goldstein, & Levine, 1992; Ramsay, 1988). When Jason, Brown, et al. (2012) applied these revised criteria to a data set of patients diagnosed with CFS according to the Fukuda et al. (1994) criteria, those with ME were more functionally impaired. However, the prior studies comparing ME with CFS had several limitations, including the fact that the patients were all selected by initially meeting the CFS Fukuda et al. (1994) criteria and were from one urban area in the United States.

In the present study, we applied the ME criteria to two data sets, one from the United States and one from Great Britain. In addition, for both data sets, the current study did not rely upon individuals meeting the CFS criteria initially. We hypothesized that the ME case definitions would identify individuals with more serious symptoms and greater functional disability than those meeting the Fukuda criteria.

Method

Research Participants

Samples were generated using two distinct case ascertainment methods. The *DePaul sample* involved a convenience sample of adults self-identifying as having ME, CFS or Myalgic Encephalomyelitis/chronic fatigue syndrome (ME/CFS).

The *Newcastle Sample* involved patients referred to the Newcastle-upon-Tyne Royal Victoria Infirmary from primary care. These patients were given a complete medical work up. Therefore, the cases in these samples were obtained from two different methods of patient recruitment that are currently used in studies of this illness.

DePaul Sample—An international convenience sample of adults self-identifying as having CFS, ME/CFS, or ME were recruited. To be eligible, an individual needed to be between the ages of 18 and 65, capable of reading and writing English, and have a self-reported current diagnosis of CFS, ME/CFS, or ME. Following approval by DePaul University's Institutional Review Board, participants were recruited from a variety of sources, such as posting on internet forums, visiting support groups, re-contacting individuals who had participated in the DePaul ME/CFS Research Team's studies in the past and had indicated interest in future studies, and contacting individuals who had emailed the team's address in the past with interest in future studies. Participants were then given three options for completion of the surveys: an electronic survey, a hard-copy survey, or a verbal survey over the telephone. All participants were given the opportunity to complete these surveys at home or in person at the Center for Community Research at DePaul University. Participants were not given a timeline for survey completion, as this illness can be unpredictable and result in a rapid decline of functioning on any given day. The first 100 individuals who completed the survey received a \$5.00 gift card to [Amazon.com](https://www.amazon.com) for their participation.

Of the original 217 individuals who completed the DSQ, 189 participants were included in the present study. Twenty-eight participants were excluded due to active medical or psychological conditions that preclude a diagnosis of CFS based upon the universally accepted Fukuda et al. (1994) case definition, or due to endorsing lifelong fatigue, also exclusionary under the Fukuda et al. (1994) case definition.

Demographically, the sample of 189 participants was 83.5% female and 16.5% male. 97.9% of the sample identified as Caucasian, 0.5% as Asian, and the remaining 1.6% identified as "Other." 55.3% of the sample stated that they were currently on disability, with only 12.8% of the sample working part or full-time. With regards to educational level, 39.9% of the sample held a professional degree, 35.6% held a standard college degree, 17.6% attended college for at least one year, and 6.9% completed high school or had a GED. The mean age was 51.6 ($SD= 11.2$).

Newcastle Sample—Individuals were consecutive patients referred to the Newcastle-upon-Tyne Royal Victoria Infirmary from primary care. They excluded those with a number of serious psychiatric disorders and other confounding medical conditions such as cancer. A total of 96 participants were included in this study (4 participants were excluded for morbid obesity or endorsing lifelong fatigue). Primary care physicians referred patients with a suspected diagnosis of CFS for complete medical assessment at Newcastle-upon-Tyne Royal Victoria Infirmary. At the infirmary, an experienced consultant physician performed a comprehensive medical history and examination. To be included in the study, blood parameters as described in the Nice Clinical guidelines (2007) had to be met. Participants also completed the Hospital Anxiety and Depression Scale (Zigmond, & Snaith, 1983).

Those who met eligibility criteria completed a written informed consent process before being included in the sample. They completed the study measures by hard copy.

The Newcastle sample was 99% Caucasian and 1% multiracial, and 81.3% of participants were female. Of this sample, 36.1% of participants were working either part- or full-time, and 30.2% were on disability. With regard to education level, 18.8% had a graduate or professional degree; 28.1% had a college degree; 20.8% had completed at least one year of college; 13.5% had a high school degree; and 11.5% had not completed high school. The average age of the sample was 46 ($SD=14.2$).

Measures

The DePaul Symptom Questionnaire—All participants completed the DePaul Symptom Questionnaire (DSQ) (Jason, Evans, et al., 2010), a self-report measure of CFS, ME/CFS and ME symptomatology, demographics, and medical, occupational and social history. The DSQ has items that tap the dimensions of the Fukuda et al. (1994) CFS case definition, the ME/CFS case definition (Carruthers et al., 2003), and the ME case definition (Jason, Damrongvachiraphan, et al., 2012). Participants were asked to rate each symptom's frequency over the past 6 months on a 5-point Likert scale for which 0=none of the time, 1=a little of the time, 2=about half the time, 3=most of the time, and 4=all of the time. Likewise, participants were asked to rate each symptom's severity over the past 6 months on a 5-point Likert scale for which 0=symptom not present, 1=mild, 2=moderate, 3=severe, 4=very severe. Both ratings of frequency and severity had to be 2 or higher in order to qualify for each individual symptom to meet criteria. The development of the DSQ was also based upon the CFS Questionnaire, which evidences good inter-rater and test-retest reliability, and was able to sensitively distinguish between those with CFS, individuals with Major Depressive Disorder and healthy controls (Hawk, Jason & Torres-Harding, 2006). The CFS Questionnaire also assesses for frequency and severity over the past 6 months, but the severity rating is on a scale from 0–100 whereas the DSQ has a Likert scale. The CFS Questionnaire was not developed to tap the ME criteria, whereas the DSQ was developed to assess these criteria. To facilitate comparison between the DSQ symptom scores and the CFS Questionnaire symptom scores, the DSQ frequency and severity scores were multiplied by 25 to obtain a 100-point scale. For each symptom, the frequency and severity ratings were then averaged to obtain a composite score.

Functional status

Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36or RAND Questionnaire)—The SF-36 is a 36-item self-report measure of functional status related to health (Ware & Sherbourne, 1992). A higher score indicates better health or less impact of health on functioning. An example of a question on this form follows: Does your health now limit you in these activities? Walking one block (Yes, limited a lot; Yes, limited a little; No, not limited at all). Test construction studies for the SF-36 (McHorney, Ware, Lu, & Sherbourne, 1994) have shown adequate internal consistency, significant discriminate validity among subscales, and substantial differences between patient and non-patient populations in the pattern of scores.

Case Definitions

CFS Case Definition (Fukuda et al., 1994)—A case of chronic fatigue syndrome is defined by Fukuda et al. (1994) as the presence of the following criteria: (1) clinically evaluated, unexplained, persistent or relapsing chronic fatigue that is of new or definite onset (has not been lifelong); is not the result of ongoing exertion; is not substantially alleviated by rest and results in substantial reduction in previous levels of occupational, educational, social, or personal activities, and (2) the concurrent occurrence of four or more of the following symptoms, all of which must have persisted or recurred during 6 or more consecutive months of illness and must not have predated the fatigue: memory or concentration problems, sore throat, tender lymph nodes, muscle pain, joint pain, headaches, unrefreshing sleep, and post-exertional malaise (Fukuda et al., 1994, p.956).

ME Case Definition—We created a revised case definition for ME (Jason, Damrongvachiraphan, et al., 2012) based on past case definitions, which include the Ramsay (1988) definition, the Dowsett et al. (1994) “London” criteria, the Hyde (2007) Nightingale definition, and the Goudsmit et al. (2009) criteria. Specifically, we used past case definitions to create a revised criteria based on the cardinal features of ME. The revised definition stipulates that ME had an acute onset that could be categorized into three categories: ME-viral (ME was precipitated by a virus), ME-infectious non-viral (ME was precipitated by a non-viral infection such as a tick bite), and ME-other (ME was precipitated by trauma or chemical exposure). These categorizations were based upon patients’ self-report symptom histories. Patients also categorized their onset as sudden or gradual. Additionally, they were asked: “Over what period of time did your fatigue related illness develop?” The responses included the following answers: within 24 hours, over 1 week, over 1 month, over 2–6 months, etc. To meet ME sudden onset criteria, patients needed to indicate a sudden onset and that their illness developed either within 24 hours or over 1 week.

The major symptom categories of ME in the revised case definition included: post-exertional malaise, neurological manifestations, and autonomic dysfunction. Post-exertional malaise was described as prolonged restoration of muscle power following either mental or physical exertion with recovery often taking 2–24 hours or longer. Neurological manifestations included at least one of the following symptoms: short-term memory loss, loss of concentration, cognitive dysfunction, increased irritability, confusion, and perceptual difficulties. Autonomic dysfunction included at least one of the following: neutrally mediated hypotension, postural orthostatic tachycardia, delayed postural hypotension, palpitations with or without cardiac arrhythmias, dizziness, feeling unsteady on ones feet, disturbed balance, cold extremities, hypersensitivity to climate change, cardiac irregularity, Raynaud’s phenomenon, circulating blood volume decrease, and shortness of breath. Secondary features of ME included: pain, endocrine manifestations, immune manifestations, and sleep dysfunction. To meet full criteria of ME, patients must have had an acute onset and qualify for the three major ME symptom categories (post-exertional malaise, neurological manifestations, and autonomic manifestations).

Results

Demographics

Table 1 presents demographic, psychiatric, and illness onset data for those meeting the ME versus CFS criteria. There was one significant demographic difference in the Newcastle sample regarding level of education [$p = 0.02$, Fisher's exact test]. As expected, the ME condition had significantly more reports of sudden onset than the Fukuda CFS condition in both samples (DePaul Sample: [$\chi^2(6, N = 181) = 111.72, p < 0.001$]; Newcastle Sample: [$\chi^2(6, N = 78) = 71.96, p < 0.01$]).

Functional Status

Table 2 presents data from the SF-36. For the DePaul sample, results of a MANOVA indicated that the ME group was significantly different than the CFS group [Wilks' Lambda = 2.53, $F(7, 170) = 3.53, p = .01$]. Because of a violation of MANOVA assumptions, the MANOVA was conducted on 7 of the 8 subscales, and a separate ANOVA was conducted to confirm the results of the remaining subscale (Role Physical). Upon examination of the univariate tests, the ME condition had significantly worse scores than the CFS group on the following subscales: Physical Functioning [$F(1, 176) = 8.16, p = .01$], Role Physical [$F(1, 180) = 5.42, p = .02$], and Bodily Pain [$F(1, 176) = 8.24, p = .01$].

For the Newcastle sample, individual ANOVAs were conducted due to the smaller sample size. Results indicate that the ME group had significantly worse scores for the General Health subscale [$F(1, 80) = 5.38, p = .02$]. Although they were not significantly different, mean scores were directionally worse for the Physical Functioning, Role Physical, and Bodily Pain subscales, as seen in the DePaul sample.

Symptoms

Table 3 lists the symptoms for the CFS and ME groups. The symptoms are categorized into the following groups: Fatigue, Post-Exertional Malaise, Pain, Neurological, Autonomic, Neuroendocrine, and Immune. For the DePaul sample, MANOVAs were conducted for each symptom group. The ME and CFS groups were significantly different in the post-exertional malaise category [Wilks' Lambda = .93, $F(5, 170) = 2.41, p = .04$]. The univariate tests reveal that the ME group had significantly worse scores for the following post-exertional malaise items: soreness after non-strenuous activity [$F(1, 174) = 7.15, p = .01$], minimum exercise makes you physically tired [$F(1, 174) = 9.03, p < .01$], and feeling drained or sick after mild activity [$F(1, 174) = 6.95, p = .01$]. Although not significantly different, the ME group in the Newcastle sample showed directionally worse scores for these items as well.

Individual ANOVAs were conducted for each symptom in the Newcastle sample. Given the number of comparisons and risk of Type I error, differences found at the $p < .01$ level can be interpreted with more confidence than those at the $p < .05$ level. One symptom, nausea, was significantly different at the $p < 0.01$ level [$F(1, 80) = 8.05, p = .01$].

Discussion

The current study confirms findings from Jason, Brown et al. (2012), which found that the ME criteria (as defined by Jason, Damrongvachiraphan, et al., 2012) selected a smaller group of individuals that had more severe functional limitations as well as more severe post-exertional malaise symptoms than those meeting the CFS criteria. Using two separate samples, from the United States and Great Britain, those who met the ME criteria proposed by Dowsett et al. (1994), Goudsmit et al. (2009) and Ramsay (1988) were a more homogenous group, with more impairment. The ME criteria requires four symptoms, as does the Fukuda et al. (1994) criteria; however, the ME criteria was more specific requiring an acute onset and three major ME symptom categories (post-exertional malaise and neurological and autonomic manifestations).

An advantage of the current study, in addition to having two samples, was that the participants were not first identified as having the Fukuda et al. (1994) CFS case definition; however, 96.3% of the DePaul sample and 87.6% of the Newcastle sample met the CFS criteria. Conversely, only 24% of the DePaul sample and 19.1% of the Newcastle sample met the ME criteria. The prior study by Jason, Brown et al. (2012) found that only 24% of their sample also met the ME criteria. The comparability of these two samples is indicative of the reliability of this case definition and the more selective nature of the four ME criteria. In addition to including a smaller percentage of patients, this ME criteria selects a more impaired group.

Table 2 indicates that both ME groups had more impairment than the CFS groups. Similarly, Table 3 shows that the ME groups had worse post-exertional malaise symptoms than the CFS groups. These data add evidence that requiring specific criteria, as the ME case definition does, selects individuals with more functional disabilities and symptoms.

Several studies have used statistical techniques to determine the factor structure of items with patients having this illness. For example, Friedberg, Dechene, McKenzie and Fontanetta (2000) found a three-factor solution including: cognitive problems, flu-like symptoms, and neurologic symptoms. Jason, Corradi and Torres-Harding (2007) found a six-factor solution including: neurocognitive, vascular, inflammation, muscle/joint, infectious, and sleep/post-exertional malaise symptoms. Arroll and Senior (2009) found a five-factor solution including Fibromyalgia syndrome-like, depression/anxiety, fatigue/post-exertional malaise, cognitive/neurological, and irritable bowel syndrome-like symptoms. Hickie et al. (2009) found a five-factor model involving musculoskeletal pain/fatigue, neurocognitive difficulties, inflammation, sleep disturbance/fatigue, and mood disturbance. Brown and Jason (2013) found the following three factors: neuroendocrine, autonomic, and immune dysfunction; neurological/cognitive dysfunction; and post-exertional malaise. It is clear from these studies that many have post-exertional malaise, neurocognitive impairments, and autonomic dysfunction, as specified in the ME criteria. In contrast, the Canadian ME/CFS (Carruthers et al., 2003) and the ME-ICC (Carruthers et al., 2011) specify many more symptom clusters that must be present for a diagnosis.

The Fukuda et al. (1994) CFS case definition has been extensively used by researchers for the past two decades. Unfortunately, it is possible that some patients meeting these criteria do not have core symptoms such as post-exertional malaise or memory/concentration problems. The ME criteria did identify a smaller subset of patients with more severe functional impairment and post-exertional malaise symptoms. These converging findings provide evidence supporting the ME construct as proposed earlier (Dowsett et al., 1994; Goudsmit et al., 2009; Ramsay, 1988).

Over time, there have been a number of terms and criteria used including CFS (operationalized by using the Fukuda et al., 1994 or Reeves et al., 2005 criteria), ME/CFS (operationalized by using the Canadian criteria of Carruthers et al., 2003), or ME (Ramsay, 1988; operationalized by using guidelines specified by Carruthers et al., 2011 or Jason, Damrongvachiraphan, et al., 2012). As more researchers begin to use different case definitions and criteria to select samples, it is imperative to specify which criteria researchers are using so that findings can be better compared (Jason, Unger et al., 2012). Future research needs to be directed at continuing to compare and contrast current case definitions, operationalizing current criteria to reduce criterion variance, and using more sophisticated analytic structures to determine critical dimensions (Jason, Skendrovic, et al., 2012).

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Table 1**Demographics, Psychiatric Characteristics, and Onset Issues**

	DePaul Sample				Newcastle Sample			
	CFS		ME		CFS		ME	
	M (SD)	N (%)	M (SD)	N (%)	M (SD)	N (%)	M (SD)	N (%)
Age	52.5 (11.5)	49 (6)	49.6 (10.7)	45 (3)	45.3 (13.5)	48 (4)	48.4 (14.2)	
Other Demographic Information:								
	N (%)	N (%)	N (%)	Sig.	N (%)	N (%)	N (%)	Sig.
Gender								
Male	19 (15)	11 (20)	11 (17)		5 (29)			
Female	106 (85)	45 (80)	55 (83)		12 (71)			
Race								
Caucasian	122 (97)	55 (100)	65 (98)		17 (100)			
Asian / Pacific Islander	1 (1)	0 (0)	0 (0)		0 (0)			
Other	3 (2)	0 (0)	1 (2)		0 (0)			
Marital status								
Married / Living with partner	74 (60)	28 (51)	33 (50)		11 (65)			
Separated	1 (1)	0 (0)	2 (3)		0 (0)			
Divorced	19 (15)	13 (24)	10 (15)		2 (12)			
Never married	29 (24)	14 (25)	21 (32)		4 (24)			
Work status								
On disability	61 (48)	40 (73)	23 (35)		6 (35)			
Student	6 (5)	0 (0)	3 (5)		1 (6)			
Homemaker	7 (6)	2 (4)	1 (2)		0 (0)			
Retired	19 (15)	3 (5)	11 (17)		3 (18)			
Unemployed	16 (13)	6 (11)	2 (3)		3 (18)			
Working part-time	11 (9)	3 (5)	15 (23)		2 (12)			
Working full-time	6 (5)	1 (2)	10 (15)		2 (12)			
Educational level								
Less than high school	0 (0)	0 (0)	2 (3)		0 (0)			*
Some high school	0 (0)	0 (0)	6 (10)		1 (7)			

High school	8 (6)	5 (9)	7 (11)	5 (33)
Partial college	21 (17)	11 (20)	15 (24)	2 (13)
Standard college degree	44 (35)	20 (36)	17 (27)	7 (47)
Graduate / Professional degree	53 (42)	19 (35)	16 (25)	0 (0)

Psychiatric and Onset Issues:	DePaul Sample		Newcastle Sample	
	CFS N (%)	ME N (%)	CFS N (%)	ME N (%)
Lifetime psychiatric diagnosis				
Yes	54 (43)	23 (41)	28 (42)	6 (35)
No	72 (57)	33 (59)	38 (58)	11 (65)
Time period of illness onset				
Within 24 hours	13 (10)	34 (62)	0 (0)	6 (43) ***
Over 1 week	7 (6)	21 (38)	1 (2)	8 (57)
Over 1 month	23 (18)	0 (0)	3 (5)	0 (0)
Over 2–6 months	29 (23)	0 (0)	19 (30)	0 (0)
Over 7–12 months	10 (8)	0 (0)	10 (16)	0 (0)
Over 1–2 years	19 (15)	0 (0)	11 (17)	0 (0)
Over 3 or more years	25 (20)	0 (0)	20 (31)	0 (0)
Cause of fatigue:				
Definitely physical	95 (77)	47 (85)	32 (55)	11 (69)
Mainly physical	22 (18)	7 (13)	14 (24)	2 (13)
Equally physical and psychological	7 (6)	1 (2)	11 (19)	3 (19)
Mainly psychological	0 (0)	0 (0)	1 (2)	0 (0)
Definitely psychological	0 (0)	0 (0)	0 (0)	0 (0)

Table 2

SF-36 Subscales (Higher score indicates less impairment)

	DePaul Sample			Newcastle Sample		
	CFS M (SD)	ME M (SD)	Sig.	CFS M (SD)	ME M (SD)	Sig.
Physical Functioning	32.1 (18.8)	23.8 (16.4)	**	34.8 (27.7)	24.6 (18.7)	
Role Physical	6.1 (17.4)	1.8 (8.1)	*	9.4 (18.6)	5.9 (18.8)	
Bodily Pain	44.4 (23.6)	34.2 (18.6)	**	33.2 (22.2)	26.8 (23.5)	
General Health	26.2 (15.2)	22.9 (12.0)		24.9 (15.3)	15.9 (8.3)	*
Social Functioning	21.9 (19.8)	15.8 (19.4)		28.4 (20.9)	22.8 (22.2)	
Mental Health	71.0 (17.0)	73.4 (16.4)		58.8 (20.5)	66.7 (18.9)	
Role Emotional	77.3 (39.1)	85.1 (31.7)		61.9 (44.3)	62.5 (45.3)	
Vitality	13.3 (13.5)	12.2 (12.2)		15.1 (14.5)	13.2 (15.1)	

 $p < 0.01$;*
 $p < 0.05$

Table 3

Symptoms (Higher score indicates **more** impairment)

	DePaul Sample				Newcastle Sample			
	CFS M (SD)	ME M (SD)	Sig.		CFS M (SD)	ME M (SD)	Sig.	
Fatigue	78.3 (16.6)	81.9 (14.3)			77.9 (14.8)	83.1 (14.6)		
Post-exertional malaise								
Dead, heavy feeling after starting to exercise	66.4 (28.4)	72.0 (30.4)			70.2 (25.0)	72.7 (27.8)		
Next-day soreness after non-strenuous activities	71.7 (20.6)	80.6 (19.4)	**		70.5 (25.4)	77.2 (17.8)		
Mentally tired after slightest effort	60.7 (26.0)	68.3 (21.3)			66.8 (25.6)	69.1 (24.3)		
Minimum exercise makes you tired	72.3 (24.8)	83.6 (17.6)	**		69.4 (23.4)	77.9 (23.2)		
Physically drained / sick after mild activity	68.8 (25.1)	78.9 (19.8)	**		65.0 (27.5)	69.1 (25.4)		
Sleep								
Unrefreshing sleep	77.9 (20.8)	79.9 (22.4)			83.1 (16.5)	83.8 (17.5)		
Need to nap during each day	52.1 (31.1)	49.5 (29.5)			47.9 (32.6)	63.2 (34.4)		
Problems falling asleep	57.8 (33.1)	63.7 (28.4)			53.5 (32.4)	48.5 (34.5)		
Problems staying asleep	63.3 (29.3)	58.6 (32.7)			49.2 (30.7)	53.1 (36.9)		
Waking up early in the morning	50.3 (32.1)	44.9 (34.7)			42.7 (29.3)	55.1 (39.3)		
Sleeping all day / staying awake all night	14.6 (25.5)	21.3 (30.5)			17.2 (25.7)	19.9 (23.0)		
Pain								
Muscle pain	58.8 (27.5)	67.7 (23.0)			71.4 (22.8)	81.6 (20.8)		
Pain in multiple joints	50.4 (33.5)	51.8 (33.0)			65.4 (28.5)	76.5 (25.7)		
Eye pain	32.7 (28.2)	33.0 (29.6)			39.2 (28.2)	44.1 (25.4)		
Chest pain	23.7 (24.4)	30.7 (25.2)			28.7 (25.6)	26.5 (25.3)		
Bloating	44.7 (30.0)	45.0 (24.5)			41.0 (32.2)	51.5 (29.9)		
Abdomen / stomach pain	38.5 (26.5)	36.8 (24.3)			37.7 (32.2)	55.1 (28.0)	*	
Headaches	47.1 (24.9)	53.4 (25.7)			59.6 (24.1)	63.2 (27.4)		
Neurocognitive								
Muscle twitches	33.8 (25.9)	26.0 (24.6)			37.5 (30.5)	42.6 (32.8)		
Muscle weakness	60.0 (27.0)	64.7 (28.3)			64.4 (25.2)	76.5 (23.8)		
Sensitivity to noise	59.8 (28.9)	65.2 (26.1)			52.7 (33.7)	61.8 (27.1)		

	DePaul Sample				Newcastle Sample			
	CFS	ME	Sig.		CFS	ME	Sig.	
	M (SD)	M (SD)			M (SD)	M (SD)		
Sensitivity to bright lights	54.3 (29.5)	63.5 (28.0)			50.4 (30.1)	61.0 (28.6)		
Problems remembering things	66.4 (21.2)	64.7 (23.8)			69.0 (23.1)	75.7 (19.0)		
Difficulty paying attention for long periods of time	71.1 (27.1)	75.0 (20.3)			73.0 (21.6)	82.4 (18.3)		
Difficulty expressing thoughts	62.8 (23.7)	59.6 (24.4)			61.0 (26.4)	70.6 (19.7)		
Difficulty understanding things	45.7 (24.8)	50.0 (19.7)			54.2 (27.3)	60.2 (28.9)		
Can only focus on one thing at a time	66.7 (29.7)	73.3 (22.2)			64.6 (25.8)	72.8 (24.3)		
Unable to focus vision / attention	47.2 (26.9)	53.9 (21.0)			50.8 (27.2)	53.7 (22.4)		
Loss of depth perception	25.1 (30.7)	25.2 (32.8)			27.0 (31.2)	39.2 (38.6)		
Slowness of thought	57.8 (24.4)	59.8 (23.1)			57.8 (26.3)	61.8 (21.9)		
Absent-mindedness	60.1 (25.8)	59.3 (28.9)			60.0 (28.1)	73.5 (20.7)		
Autonomic								
Bladder problems	29.4 (33.3)	31.8 (31.0)			26.6 (31.0)	42.6 (34.8)		
Irritable bowel problems	44.1 (32.4)	48.8 (28.8)			46.5 (33.5)	64.1 (35.9)		
Nausea	31.3 (24.5)	33.7 (23.1)		**	33.7 (25.5)	52.9 (22.8)		
Feeling unsteady on feet	39.5 (25.3)	46.5 (28.9)			45.4 (28.1)	52.9 (29.8)		
Shortness of breath	36.6 (27.5)	43.4 (23.3)			34.9 (25.8)	39.0 (33.3)		
Dizziness / fainting	35.9 (24.6)	44.3 (26.1)			46.6 (28.9)	39.0 (30.9)		
Irregular heart beats	30.5 (27.1)	32.5 (27.6)			33.7 (31.8)	37.5 (32.2)		
Neuroendocrine								
Losing / gaining weight without trying	38.9 (34.6)	37.0 (34.4)			45.9 (34.5)	48.5 (38.0)		
No appetite	22.5 (24.5)	22.1 (21.3)			24.6 (29.3)	43.4 (31.6)		*
Sweating hands	13.4 (23.0)	6.6 (13.5)			21.9 (29.9)	19.5 (27.0)		
Night sweats	35.3 (31.4)	31.4 (29.8)			34.1 (30.2)	39.0 (30.6)		
Cold limbs	53.0 (30.5)	49.5 (30.9)			49.8 (33.9)	59.6 (31.4)		
Chills / shivers	34.9 (29.0)	36.5 (25.8)			36.5 (30.2)	36.8 (31.7)		
Feeling hot / cold for no reason	50.4 (29.2)	52.9 (27.9)			56.1 (28.7)	51.5 (29.6)		
Feeling like you have a high temperature	28.7 (28.2)	38.0 (32.8)			39.7 (32.4)	45.6 (31.9)		
Feeling like you have a low temperature	25.7 (29.6)	34.1 (28.5)			22.0 (29.3)	33.1 (32.2)		
Alcohol intolerance	46.3 (39.6)	53.9 (39.6)			45.0 (36.0)	55.0 (40.0)		

	DePaul Sample			Newcastle Sample		
	CFS	ME	Sig.	CFS	ME	Sig.
	M (SD)	M (SD)		M (SD)	M (SD)	
Immune						
Sore throat	36.0 (23.3)	34.6 (24.8)		41.8 (29.1)	43.4 (30.7)	
Tender lymph nodes	38.6 (28.2)	49.0 (29.5)		39.1 (30.0)	36.8 (30.4)	
Fever	13.6 (19.4)	17.5 (22.0)		21.0 (26.5)	25.8 (24.4)	
Flu-like symptoms	49.9 (26.4)	59.1 (26.3)		54.6 (27.8)	54.4 (27.6)	
Sensitivity to smells/foods/medications/chemicals	52.8 (36.1)	58.4 (35.5)		43.1 (36.6)	53.7 (38.7)	

**
 $p < 0.01$;

*
 $p < 0.05$