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Differentiating Multiple Sclerosis from Myalgic Encephalomyelitis and Chronic Fatigue Syndrome

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Abstract

Multiple Sclerosis (MS), Myalgic Encephalomyelitis (ME), and Chronic Fatigue syndrome are debilitating chronic illnesses, with some overlapping symptoms. However, few studies have compared and contrasted symptom and disability profiles for these illnesses for the purpose of further differentiating them. The current study was an online self-report survey that compared symptoms from a sample of individuals with MS (N = 120) with a sample of individuals with ME or CFS (N = 269). Respondents completed the self-report DePaul Symptom Questionnaire. Those individuals with ME or CFS reported significantly more functional limitations and significantly more severe symptoms than those with MS. The implications of these findings are discussed.

Keywords

Chronic fatigue syndrome (CFS); Myalgic encephalomyelitis (ME); Multiple sclerosis (MS); Depaul symptom questionnaire

Introduction

Multple Sclerosis (MS) is a chronic illness that has some overlapping symptoms with Myalgic Encephalomyelitis (ME) and Chronic Fatigue Syndrome (CFS). Fatigue is a common symptom in MS, even early in the disease [1]. Two-thirds of patients with MS indicated Fatigue as one of the worst three common symptoms that they experience [2]. Shahnaz et al. [3] found the symptoms of MS often cause physical and mental dysfunction, which interferes with their ability to engage in life roles. Initially, MS was not well understood [4], with some even suggested personality characteristics such as the “MS-prone personality,’ which stigmatized patients [5]. As the medical knowledge improved, MS eventually became recognized as an authentic biological illness. The primary test for MS is MRI detection of brain lesions [3], however, in the event that MRI results are inconclusive a spinal tap and other blood tests are required for diagnosis.

Similar to early explanations for the symptoms of MS, some investigators today believe that ME and CFS are stress related or psychiatrically caused [6,7]. In part due to this

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psychogenic belief, many patients with ME and CFS feel stigmatized by this illness and often find it difficult to get medical care in order to be diagnosed and receive appropriate treatment. For example, one study found that 71% of ME and CFS patients had to visit over 4 physicians to receive a diagnosis and 63% of patients searched for over 2 years to receive a diagnosis [8]. Green et al. [9] found that 95% of females seeking medical treatment for CFS reported feelings of estrangement. Twemlow et al. [10] found that 609 surveyed patients with CFS reported a 66% higher frequency of physician-caused illness compared to a general population of medical patients. Anderson et al. [11] found that 77% of patients with CFS had negative interactions with doctors. Jason et al. [12] conducted a content analysis of 129,527 pages of medical textbooks in order to assess the frequency of CFS and MS related information. CFS content was presented on 0.06% of pages but MS was in 0.12% of pages. Even though CFS is estimated to occur at a higher prevalence than MS (.42% versus 0.09%), apparently CFS receives less attention in medical training.

There have been several attempts to identify biological markers for ME and CFS that could differentiate the condition from MS. For example, there is evidence of increased expression of pro-inflammatory cytokine IL-8 in those with CFS and MS [13], Recently, Sorenson et al. [14] examined stimulated and unstimulated cells in peripheral blood among those with CFS, MS, and controls. Compared to patients with MS and controls, CFS was characterized by a unique pattern of global immunologic activation. The relationships between the cytokines in those with CFS demonstrated a pattern of stronger correlation than unstimulated and stimulated peripheral blood mononuclear cells from control or MS samples, with a differential neighborhood association highlighting dissimilarity between MS and CFS.

Several studies have also attempted to differentiate CFS or ME from MS using self-report measures. Jason et al. [15] found that among MS, CFS and Lupus patients, those with MS were the most similar to CFS in terms of impairment due to fatigue and reductions in activity. However, this study was limited in sample sizes and did not include a large set of symptom questions. In a more recent study, Ohanian et al. [16] found that the best self-report symptoms for discriminating MS from ME or CFS were from the immune domain (i.e., flu-like symptoms and tender lymph nodes), and that decision tree analysis could correctly differentiate MS from ME or CFS 81.2% of the time. However, this study did not compare the larger group of symptoms available, nor did it examine functional differences. The current study compared patients with MS versus those with ME or CFS, and attempted to learn what symptoms and functional differences would emerge between these chronic illnesses.

Methods

Participants

Participants were 106 people with MS and 269 people with ME or CFS (excluding those with exclusionary medical or psychiatric illnesses according to Fukuda et al. [17] or Carruthers et al. [18]. They were recruited for the online study using links and descriptions of the survey posted to support group websites, national foundations, research forums, and social media outlets including Facebook and Twitter. The study obtained approval from the DePaul Institutional Review Board.

Measures

DePaul Symptom Questionnaire (DSQ)—The DSQ is a 54-item self-report measure of symptomatology. It also includes items assessing demographic, medical, occupational and social history [19]. For each symptom, participants were asked to rate their symptom frequency and severity on a scale from 0–4. For frequency: 0 = “none of the time,” 1 = “a little of the time,” 2 = “about half the time,” 3 = “most of the time,” 4 = “all of the time.” For severity: 0 = “symptom not present,” 1 = “mild,” 2 = “moderate,” 3 = “severe,” 4 = “very severe.” DSQ composite scores were calculated by multiplying both the frequency and severity scores by 25 to create 100-point scales. The 100-point frequency and severity scores for each symptom were then averaged to create one composite score per symptom. A higher composite score represents more severe symptoms. The DSQ is available at REDCap’s [20] shared library.

The DSQ has evidenced good test-retest reliability among both patient and control groups [21]. The scale has a three-factor solution, with factors evidencing good internal consistency [22]. Murdock et al. [23], an independent group using the DSQ, found that it demonstrated excellent internal reliability, and that among patient-reported symptom measures, it optimally differentiated between patients and controls.

Medical outcomes study 36-item short-form health survey (SF-36)—The SF-36 is a well validated and widely used 36-item self-report measure of health related functional status in 8 domains [24]. A higher score indicates better health or less impact of health on functioning. Respondents rate limitations experienced in relation to a variety of activities (e.g., “Does your health now limit you in these activities? Walking one block”). Test construction studies for the SF-36 have shown adequate internal consistency, significant discriminant validity among subscales, and substantial differences between patient and non-patient populations in the pattern of scores [25].

Analysis

Individuals were excluded from the analysis if they reported having medical or psychiatric illnesses that exclude a diagnosis of CFS according to Fukuda et al. and Carruthers et al. [17,18] Analysis of variance or chi-square analyses examined differences in demographic characteristics, functional status (SF-36), and symptoms (DSQ) between the two illness groups. Due to unequal sample sizes and variances, Welch’s F tests and Games-Howell post hoc tests were conducted to compare the SF-36 scores and composite scores for individual DSQ symptoms.

Results

Table 1 displays sociodemographic differences between the samples. The ME and CFS group was older, more Caucasian, and less likely to be married. A greater proportion of the ME and CFS group were on disability or not working compared to the MS group, but this was considered more of an outcome variable, differentiating the two groups. Except for marital and working status, effect sizes were modest for differences in participant background characteristics. Analyses were conducted using covariates that differentiated the

groups, however, when doing so model results were comparable and for this reason we present the results in Tables 2 and 3 without covariates.

Table 2 shows SF-36 differences between the samples. On most subscales, the ME and CFS group evidenced greater functional limitations than the MS group. Significant differences were found for Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, and Social Functioning. No significant differences were found for the Role Emotional and Mental Health subscales.

Table 3 provides symptom data across the two chronic illness groups. Similar to the SF-36 data, those in the ME and CFS group were significantly more symptomatic on almost all variables. In comparison to the MS group, the ME and CFS group had significantly worse functioning on the fatigue item, all 9 post-exertional malaise items, 2 sleep items, all 10 pain items, 11 neurocognitive items, 9 autonomic items, 11 neuroendocrine items, 5 immune items, and both of the 2 other items. For those symptoms without significant differences across groups, the ME and CFS group had scores that trended toward more severity than the MS group. This was the case for all items except the following 4 symptoms: daytime drowsiness, muscle twitches, bladder problems, and urgent need to urinate.

Discussion

This study found that patients with MS and those with ME and CFS have significant functional limitations and high levels of somatic symptoms. However, those with ME or CFS evidenced greater impairment on SF-36 sub-scales as well as most of the DSQ symptoms. In our sample, those with ME and CFS also reported particularly high levels of disability and low levels of work status. These findings provide further evidence for health care professionals of the seriousness of ME and CFS.

Even though the group with ME or CFS reported greater disability, less full or part-time work, and more functional limitations than the MS group, it is of interest that there were not significant differences on the role emotional or mental health subscales. This suggests that with a great illness burden, and continuing skepticism about the legitimacy of ME and CFS, those with this illness tend to be functioning relatively well on mental health related indices.

In a prior study by Ohanian et al. [16], immune symptoms were the best DSQ items for differentiating those with MS from those with ME or CFS. This is of interest as immune functioning is not a required symptom of the new IOM clinical criteria [26]. Previous research has established evidence of immune functioning problems in ME and CFS populations [27,28]. However, the current study indicates that beyond immune dysfunction, multiple symptom domains from the DSQ differentiate those with MS from those with ME and CFS. Nonetheless, a medical examination is still critical to make definitive differentiations among these chronic illnesses.

Several limitations are worth noting. The web based implementation of our survey materials made it more difficult for individuals to participate if they did not have a computer or were not able to access the Internet. Also, because we did not have an independent medical assessment of individuals, and diagnoses were self-reported, it is possible that some

participants did not have either MS or ME or CFS, or that participants had additional conditions that might be exclusionary for ME or CFS. In addition, these data are based on self-report, and it would be important to confirm such findings with both immune functioning and other biological measures, as has recently been done by Sorenson et al. [14]. Finally, had we been able to follow-up with participants for an additional assessment, we might have been able to better understand change in functioning over time.

Conclusion

In summary, it is apparent that both patient groups have many serious symptoms and functional limitations. This has epidemiologic significance, as both illnesses affect many Americans, with CFS prevalence rates of 0.42% versus MS rates of 0.09%; [12]. In addition, some patients have both sets of symptoms, with some estimating that 14% of patients with MS [29] have the CFS Fukuda et al. [18] symptoms. However, these are distinct illnesses, as MS represents an exclusionary illness for a CFS diagnosis. The finding that ME and CFS group had more functional limitations and more serious symptoms than those with MS provides additional evidence to the seriousness of ME and CFS. Continued research to further compare ME and CFS with other chronic conditions can inform improved methods for differentiating the conditions for the purpose of diagnoses, treatment, and understanding etiology.

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Table 1

Demographic comparisons.

Demographic characteristics	MS (n = 120)		ME and CFS (n = 268)		Sig.
	M	(SD)	M	(SD)	
Age	44.8	(11.3)	48.6	(16.2)	**
	%	(n)	%	(n)	Sig.
Gender					
Female	84	(97)	90	(238)	–
Male	16	(19)	10	(26)	
Race					**
Caucasian	92	(109)	97	(258)	
Black, African American	3	(4)	0	(0)	
Asian, Pacific Islander	0	(0)	1	(2)	
Other	4	(5)	3	(7)	
Latno / Hispanic Origin					*
No	92	(109)	98	(259)	
Yes	8	(9)	2	(6)	
Marital Status					**
Married	66	(79)	48	(128)	
Never married	24	(28)	30	(80)	
Divorced	8	(10)	18	(48)	
Separated	2	(2)	2	(6)	
Widowed	0	(0)	2	(6)	
Education					
Some high school	0	(0)	3	(7)	
High school degree	8	(9)	7	(19)	
Partial college	28	(34)	23	(61)	
College degree	33	(39)	28	(74)	
Graduate degree	32	(38)	40	(107)	

Demographic characteristics	MS (n = 120)		ME and CFS (n = 268)		Sig.
	M	(SD)	M	(SD)	
Work Status					***
On disability	26	(31)	52	(138)	
Working part-time	13	(16)	14	(36)	
Working full-time	49	(58)	8	(20)	
Retired	3	(4)	11	(29)	
Unemployed	3	(4)	10	(26)	
Homemaker	3	(3)	5	(12)	
Student	3	(3)	2	(4)	

* p<0.05;

** p<0.01;

*** p<0.001

Table 2

SF-36 comparisons between groups.

Variables (Subscale)	MS (n = 87)		ME and CFS (n = 224)		Sig.
	M	(SD)	M	(SD)	
Physical Functioning	54.1	(27.9)	26.2	(20.3)	***
Role Physical	20.7	(31.0)	2.4	(8.7)	***
Bodily Pain	56.5	(26.7)	36.0	(24.5)	***
General Health	43.9	(21.8)	24.1	(15.0)	***
Vitality	26.3	(18.0)	10.1	(12.3)	***
Social Functioning	54.0	(26.9)	19.8	(20.8)	***
Role Emotional	54.0	(42.0)	68.6	(41.9)	–
Mental Health	69.3	(17.4)	65.9	(18.9)	–

*** p<0.001

Table 3

DSQ symptoms comparison between groups.

Symptoms	MS (n = 120)		ME and CFS (n = 269)		
	M	(SD)	M	(SD)	Sig.
Fatigue	65.6	(21.7)	81.6	(14.7)	***
Post-exertional malaise					
Dead, heavy feeling after starting to exercise	51.2	(30.4)	77.8	(23.3)	***
Next-day soreness after everyday activities	45.8	(27.8)	76.8	(19.9)	***
Mentally tired after the slightest effort	46.6	(26.5)	68.9	(22.0)	***
Physically tired after minimum exercise	52.3	(27.7)	78.5	(20.4)	***
Physically drained or sick after mild activity	46.7	(27.2)	73.2	(21.5)	***
Muscle Fatigue after mild physical activity	48.9	(29.9)	72.4	(25.1)	***
Worsening of symptoms after mild physical activity	47.6	(31.9)	78.4	(22.3)	***
Worsening of symptoms after mild mental activity	31.0	(28.8)	61.5	(27.3)	***
difficulty reading after mild physical or mental activity	14.1	(23.0)	45.6	(33.4)	***
Sleep					
Unrefreshing sleep	63.1	(26.2)	81.7	(19.5)	***
Need to nap daily	48.5	(31.0)	57.1	(30.9)	–
Problems falling asleep	42.5	(33.0)	59.7	(29.3)	***
Problems staying asleep	50.4	(33.6)	60.6	(29.5)	–
Waking up early in the morning (e.g. 3 AM)	42.7	(32.5)	49.8	(31.0)	–
Sleeping all day and staying awake all night	12.4	(23.0)	19.5	(28.8)	–
Daytime drowsiness	60.8	(27.8)	60.3	(27.1)	–
Pain					
Pain or aching in muscles	50.9	(31.6)	68.3	(26.4)	***
Joint pain	41.4	(31.8)	57.1	(33.3)	***
Eye pain	20.2	(25.0)	31.3	(28.6)	***
Chest pain	8.2	(16.0)	24.6	(23.6)	***
Bloating	27.8	(28.4)	47.2	(28.9)	***

Symptoms	MS (n = 120)		ME and CFS (n = 269)		Sig.
	M	(SD)	M	(SD)	
Abdomen / stomach pain	19.2	(22.4)	42.5	(28.1)	***
Headaches	40.9	(28.0)	52.3	(25.1)	***
Aching of the eyes or behind the eyes	22.5	(25.4)	37.0	(29.3)	***
Sensitivity to pain	28.1	(31.6)	50.1	(33.9)	***
Myofascial pain	15.1	(27.4)	29.2	(35.2)	***
Neurocognitive					
Muscle twitches	40.5	(27.5)	33.8	(25.4)	–
Muscle weakness	55.2	(30.2)	64.6	(26.3)	–
Sensitivity to noise	32.0	(30.1)	62.2	(26.8)	***
Sensitivity to bright lights	31.0	(28.4)	55.6	(29.1)	***
Problems remembering things	51.0	(30.0)	67.2	(23.8)	***
difficulty paying attention for a long period of time	46.9	(29.5)	70.0	(23.5)	***
difficulty expressing thoughts	45.0	(28.5)	60.7	(24.6)	***
difficulty understanding things	32.4	(29.9)	49.0	(24.8)	***
Can only focus on one thing at a time	41.3	(30.9)	66.1	(24.6)	***
Unable to focus vision and/or attention	35.7	(26.8)	49.7	(24.2)	***
Loss of depth perception	19.2	(28.1)	23.6	(29.3)	–
Slowness of thought	41.2	(30.2)	57.6	(26.1)	***
Absent-mindedness or forgetfulness	46.5	(30.4)	60.5	(24.4)	***
Feeling disoriented	23.5	(26.0)	35.8	(26.0)	***
Slowed speech	22.7	(26.4)	32.8	(26.8)	–
Poor coordination	44.3	(29.9)	45.9	(28.7)	–
Autonomic					
Bladder problems	35.8	(31.7)	34.9	(32.2)	–
Urgent need to urinate	42.0	(31.5)	38.8	(31.7)	–
Waking up at night to urinate	42.3	(31.5)	47.0	(31.4)	–
Irritable bowel problems	26.7	(30.4)	47.6	(32.6)	***
Nausea	16.7	(22.0)	33.3	(26.0)	***

Symptoms	MS (n = 120)		ME and CFS (n = 269)		Sig.
	M	(SD)	M	(SD)	
Feeling unsteady on feet	44.6	(29.6)	45.6	(28.7)	–
Shortness of breath	16.9	(22.2)	38.3	(26.8)	***
Dizziness or fainting	24.7	(26.4)	41.8	(28.1)	***
Irregular heartbeats	11.1	(19.4)	29.4	(26.6)	***
Heart rate increase after standing	9.1	(19.0)	45.2	(33.0)	***
Blurred or tunnel vision after standing	13.6	(21.2)	29.7	(30.6)	***
Graying or blacking out after standing	9.7	(19.5)	23.7	(28.9)	***
Inability to tolerate an upright position	15.9	(27.8)	48.0	(34.3)	***
Neuroendocrine					
Lost or gained weight without trying	26.8	(31.0)	41.4	(34.4)	***
Lack of appetite	16.4	(23.1)	29.8	(25.7)	***
Sweating hands	4.2	(13.0)	17.0	(25.6)	***
Night sweats	23.3	(28.4)	35.3	(29.9)	***
Cold limbs (e.g. arms, legs hands)	33.6	(29.7)	46.6	(29.4)	***
Chills or shivers	17.7	(21.0)	32.0	(26.5)	***
Feeling hot or cold for no reason	31.8	(29.0)	50.3	(27.1)	***
Feeling like you have a high temperature	18.4	(24.0)	32.6	(27.2)	***
Feeling like you have a low temperature	6.7	(12.8)	23.2	(25.9)	***
Alcohol intolerance	10.4	(24.8)	38.8	(38.0)	***
Intolerance to very hot or cold temperatures	63.4	(30.5)	65.7	(28.9)	–
Temperature fluctuations throughout the day	28.3	(28.6)	44.8	(30.9)	***
Immune					
Sore throat	12.7	(17.3)	36.6	(24.6)	***
Tender / sore lymph nodes	8.5	(18.5)	35.1	(29.9)	***
Fever	10.5	(17.1)	15.3	(21.6)	–
Flu-like symptoms	16.8	(22.0)	51.1	(27.3)	***
Sensitivity to smell/food/medication/chemicals	16.0	(21.2)	46.5	(33.0)	***
Viral infections with prolonged recovery periods	15.7	(26.2)	33.6	(32.1)	***

Symptoms	MS (n = 120)		ME and CFS (n = 269)		Sig.
	M	(SD)	M	(SD)	
Sinus infections	13.0	(24.7)	21.9	(26.4)	–
Others					
Sensitivity to mold	9.7	(23.3)	27.9	(36.8)	***
Sensitivity to vibrations	11.8	(20.6)	29.7	(34.3)	***

*** $p<0.001$