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An Investigation of Symptoms Predating CFS Onset

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Abstract

The Fukuda et al. (1994) criteria for chronic fatigue syndrome (CFS) specifies that a symptom can only be included within a diagnosis if it is experienced concurrently or following the onset of fatigue. In order to investigate this issue, participants provided information on persisting symptoms (lasting greater than six months) and whether those symptoms occurred prior to, concurrently, or following the onset of their fatigue. More symptoms were experienced after the fatigue onset than prior to the fatigue onset; however, a considerable number of participants reported experiencing persisting symptoms prior to the onset of CFS. Particularly, rates of hay fever and asthma were higher prior to the illness. Investigating symptoms prior to the onset of the illness might provide investigators with ways to better understand the etiology of this illness.

Keywords

Predating Symptoms; Myalgic Encephalomyelitis; chronic fatigue syndrome; Myalgic Encephalomyelitis/chronic fatigue syndrome

The Fukuda et al. (1994) case definition for chronic fatigue syndrome (CFS) requires that individuals experience six months of fatigue that is not alleviated by rest and that is of a new or definite onset and accompanied by at least four of eight symptoms (post-exertional malaise, unrefreshing sleep, memory or concentration impairment, joint pain, headaches, tender lymph nodes, and a frequent or recurring sore throat) that have also been present for at least six months. The Fukuda et al. criteria (1994) also stipulates that each of the eight case-defining symptoms are excluded from the diagnosis if they are experienced prior to the onset of the fatigue. The issue of predating symptoms has not been studied in the field to date. The Fukuda et al. (1994) definition specifically states that the fatiguing illness must be of a “new or definite onset,” and it is possible that this language infers that individuals must experience all of the CFS symptoms in a sudden manner rather than as part of a gradual progression with different symptoms appearing at different times. Fukuda et al. (1994) is not the only case definition that excludes symptoms for predating fatigue, as the earlier Holmes et al. (1988) case definition for CFS also specifies that symptoms must occur concurrently or following the onset of severe fatigue.

The language used to describe illness onset (e.g. “new” and “definite”) may have influenced the Fukuda et al. (1994) criterion specifying that symptoms must not predate the fatigue;

however, not all patients experience the illness in a sudden manner. Some individuals experience a slower progression of symptoms (DeLuca, Johnson, Ellis & Natelson, 1997), suggesting that some symptoms may appear at different times during the illness course. Consequently, excluding certain symptoms from a diagnosis due to the precedence that they not predate the CFS may be problematic. Using data derived from a larger non-pharmacological treatment study of CFS conducted by Jason et al. (2007), the present study serves as an investigation of the frequency in which symptoms are reported as occurring prior to the onset of CFS. The aim of this study is to fill a gap in our knowledge regarding symptoms experienced prior to the onset of the severe illness that has been associated with CFS.

Methods

Participants

The current study utilized baseline data derived from a larger longitudinal study of nonpharmacological treatment interventions for CFS (Jason et al., 2007). Participants were recruited from physician referrals, media advertisements, and CFS support groups. Participants were at least 18 years of age, not pregnant, able to write and speak English, and physically capable of attending scheduled appointments. Participants were included if they met the Fukuda et al. (2004) criteria for CFS as diagnosed by a physician (see Jason et al., 2007 for details on diagnostic procedures). A total of 114 participants were recruited and enrolled in the original study and their baseline data was used for the present study. All procedures were approved by the DePaul University Institutional Review Board. Informed consent was given by all participants.

Sample Characteristics

In regards to sociodemographic characteristics, 83.3% of the 114 participants were female and the average age was 43.8 years ($SD = 11.6$). Concerning ethnicity, 87.7% of the participants were White, 4.4% were African American, 4.4% were Latino, and 3.5% were Asian American. Regarding marital status, 49.1% of the participants were married/living with a partner, 33.3% were single, and 17.6% were either divorced or separated. As for work status, 40.4% of the participants were working or full-time students, and 59.6% were not working or were part-time students. Concerning education, 47.4% of the participants had earned a standard college degree, 21.8% had a graduate or professional degree, 21.1% had partial college, and 9.7% had a high school/GED degree or less.

Measures

DePaul University Fatigue Questionnaire—The DePaul University Fatigue Questionnaire is a screening scale that was initially validated by Jason et al. (1997) and is used to collect demographic, health status, medication usage, and symptom data. Hawk, Jason, and Torres-Harding (2007) later revised this CFS Questionnaire and administered it to three groups (CFS, major depressive disorder, and healthy controls) and found that the measure has good test–retest reliability as well as good sensitivity and specificity in differentiating CFS from the depressed group and healthy control group. The CFS Questionnaire was designed to assess the diagnostic criteria for CFS as specified by Fukuda

et al. (1994). For each symptom, participants were asked to indicate if the symptom had been present for six months or longer, if the symptom began before the onset of their 'fatigue or health problems,' and how often (never, seldom, often/usually, or always) the symptom is experienced. Participants were also asked to rate the severity of each symptom they endorsed on a scale of 0 to 100, where 0 = no problem and 100 = the worst problem possible. This CFS Questionnaire assesses the eight case-defining symptoms of CFS (Fukuda et al., 1994) as well as 87 additional symptoms. In assessing symptoms that predated the CFS illness, the current study utilized the item on the CFS Questionnaire that assesses whether symptoms were experienced prior to the onset of their CFS.

Analyses

All analyses were conducted using the Statistical Package for the Social Sciences (version 18.0; IBM SPSS, Chicago, IL). Descriptive analyses were conducted in order to determine the frequency and percentage of symptoms reported as occurring for six months or longer out of the 114 participants. After selecting out for the number of symptoms that persisted for six months or longer, a one sample chi-square analysis was conducted to determine whether the frequency in which each symptom was reported as occurring prior to the CFS onset was significantly different from the frequency in which each symptom was reported as occurring after or concurrently with the CFS onset.

Results

Frequencies of the symptoms assessed are displayed in Table 1. The columns from left to right display the frequency and percentage in which symptoms were reported as occurring for six months or longer, the frequency of symptoms (lasting six months) that were experienced before the CFS onset, and the frequency of symptoms (lasting six months) that were experienced concurrently or following CFS. For several symptoms, the number of predating and postdating symptoms do not include all the individuals with that particular symptom, because a few individuals did not indicate whether the symptom occurred before or after CFS onset. Only three symptoms (allergies, hay fever, and Raynaud's phenomenon) did not have significant differences between the frequency reported prior to the CFS onset versus those reported concurrent with or after CFS onset (for all other variables, significantly higher frequencies were reported for concurrent or after CFS onset). A higher percentage of hay fever symptoms (66.7 percent) and allergies (52.1 percent) were reported as occurring prior to the fatigue onset compared to concurrently or following the CFS onset (33.3 percent and 47.9 percent respectively). The second column in Table 1 lists the frequency and percentage of symptoms occurring prior to the CFS onset in descending order within each symptom category. Among the symptoms with higher pre CFS onset include: headaches, Raynaud's phenomenon, hay fever, temperature lower than normal, tense muscles, irregular periods, bloating, and anxiety/tension. A mean of 54 symptoms per participant were reported as persisting for six months or longer, and of those symptoms persisting for six months or longer, an average of seven symptoms per participant were experienced prior to the onset of CFS.

Discussion

The most widely used case definition for CFS requires symptoms be concurrent with or follow the onset of CFS (Fukuda et al., 1994), and this criterion may have originated from the language within the definition describing the illness as a “new” and “definite onset.” The current study found that significantly more symptoms were reported as experienced concurrently or following CFS compared to before. However, there were a substantial percentage of symptoms that were reported as persisting for six months or longer and experienced prior to the CFS onset. On average, participants with CFS experienced seven persisting symptoms prior to CFS onset.

Allergies and hay fever were two symptoms that were experienced before the CFS onset with higher frequency than after the CFS onset. These results are noteworthy based on recent findings revealing that a shift to a T-helper 2 (Th2) type immune response from a T-helper 1 (Th1) shift was most representative of a CFS sample (Torres-Harding, Sorenson, Jason, Maher, & Fletcher, 2008). The Th2 phenotype involves cells that secrete cytokines including IL-4, IL-5, IL-6, IL-10, IL13, and TGF- β (Schwarz et al., 2001). Interestingly IL-4 has been found to be involved in the inflammatory responses associated with allergies (Hanson, Gause, & Natelson, 2001). In light of this research, it is possible that the higher percentage of allergies and hay fever experienced prior to the onset of CFS compared to concurrently or following the CFS may point to a potential marker for the Th2 shift that is observed in individuals with this illness.

Limitations for this study include the retrospective self-report method. Participants provided self-reported information on the onset of their symptoms many months or years following the actual onset of their CFS illness; therefore, it is possible that their responses are biased due to recall difficulties that occur when remembering remote events. Furthermore, the study sample used was not selected through random assignment and thus, participants may share certain characteristics that are different from a more representative population of individuals affected by CFS. For instance, a large majority of the participants were White women and middle aged. Based on research by Jason and colleagues (1999), CFS occurs at higher rates in African American and Latino samples.

In summary, findings from the current study reveal that the majority of symptoms experienced by individuals with CFS are experienced after or concurrently with the onset of CFS; however, each symptom had a substantial percentage of participants reporting that the symptom persisted prior to the CFS onset. This finding suggests that the frequency in which symptoms are experienced prior to the CFS onset should be evaluated further in order to potentially identify certain predating symptoms as risk factors for CFS. The presence of symptoms that predate the onset of CFS may also signify different subtypes and trajectories of the illness. Furthermore, it is important to investigate possible reasons for the higher frequency in which symptoms such as allergies and hay fever are experienced prior to the CFS onset. It is recommended that future studies utilize longitudinal and prospective methods in order to track individuals' symptom experience prior to and throughout their illness development in order to eliminate the problem of recall bias that arises when using retrospective self-report measures to collect health information. Furthermore, future studies

could also compare symptom data from this study with symptoms reported in a healthy control group as well as from another chronic illness group, as different somatic symptoms are experienced with varying frequencies in the general population and within the context of other illnesses. Comparison data may shed light on the unique symptom experience of individuals with CFS. Finally, as the Fukuda et al. (1994) criteria include individuals who do not have a sudden onset, it is unclear whether it remains useful to continue excluding those symptoms that occur prior to the CFS illness, as it would be extremely difficult to determine whether a symptom occurred prior to or after the onset for those individuals with a gradual onset of CFS.

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Table 1

Percent Symptoms Predating Fatigue, Non-Pharmacological Data N=114

Symptom	6 Months % (n)	Before Fatigue % (n)	After Fatigue % (n)
<i>Fukuda Symptoms</i>			
Headaches	80.7 (92)	19.6 (18)	80.4 (74)
Sleep	100.0 (114)	15.8 (18)	84.2 (96)
Lymph Nodes	56.1 (64)	10.9 (7)	89.1 (57)
Joint Pain	71.9 (82)	8.5 (7)	91.5 (75)
Muscle Pain	91.2 (104)	7.7 (8)	92.3 (96)
Sore Throat	64.0 (73)	6.8 (5)	93.2 (68)
Memory	98.2 (112)	6.3 (7)	93.8 (105)
Post-Exertional Malaise	95.6 (109)	3.7 (4)	96.3 (105)
<i>Neurological Impairments</i>			
Poor hand to eye coordination	38.6 (44)	13.6 (6)	86.4 (38)
Attention Deficit	46.5 (53)	11.3 (6)	88.7 (47)
Order words and numbers wrong	55.3 (63)	9.5 (6)	90.5 (57)
Concentration	64.0 (83)	7.2 (6)	92.8 (77)
Slow Thought	78.1 (89)	6.7 (6)	92.2 (83)
Difficulty recalling information	83.3 (95)	6.3 (6)	93.7 (89)
Absent Mindedness	85.1 (97)	6.2 (6)	93.8 (91)
Frequently lose train of thought	74.6 (85)	5.9 (5)	94.1 (80)
Difficulty retaining information	78.1 (89)	5.6 (5)	94.4 (84)
Forgetting what trying to say	80.7 (92)	5.4 (5)	94.6 (87)
Slow to react	49.1 (56)	5.4 (3)	94.6 (53)
New trouble with math	37.7 (43)	4.7 (2)	95.3 (41)
Difficulty Comprehending Info.	62.3 (71)	4.2 (3)	95.8 (68)
Trouble expressing thoughts	73.7 (84)	3.6 (3)	96.4 (81)
Confusion/Disorientation	63.2 (72)	2.8 (2)	97.2 (70)
Concentration with Driving	42.1 (48)	0.0 (0)	100.0 (48)
<i>Sensitivities</i>			
Hay fever	26.3 (30)	66.7 (20)	33.3 (10)
Allergies	62.3 (71)	52.1 (37)	47.9 (34)
Sinus infection	49.1 (56)	33.9 (19)	66.1 (37)
Sensitivity to Alcohol	34.2 (39)	25.6 (10)	74.4 (29)
Rash	29.8 (34)	23.5 (8)	76.5 (26)
Light Sensitivity	57.0 (65)	20.0 (13)	80.0 (52)
Affected by seasonal weather	58.8 (67)	19.4 (13)	80.6 (54)
Affected by daily weather	50.9 (58)	17.2 (10)	82.8 (48)
Chemical Sensitivity	47.4 (54)	16.7 (9)	83.3 (45)
Dry mouth	55.3 (63)	11.1 (7)	88.9 (56)
Puffy face	27.2 (31)	9.7 (3)	90.3 (28)
<i>Cardiovascular</i>			

Symptom	6 Months % (n)	Before Fatigue % (n)	After Fatigue % (n)
Raynaud's Phenomenon	20.2 (23)	26.1 (6)	56.5 (13)
Shortness of Breath	60.5 (69)	18.8 (13)	81.2 (56)
Dizziness	67.5 (77)	16.9 (13)	83.1 (64)
Dizzy Standing	57.0 (65)	15.4 (10)	84.6 (55)
Light Headedness	62.3 (71)	11.3 (8)	88.7 (63)
Racing Heart	39.5 (45)	8.9 (4)	91.1 (41)
<i>Loss of Thermostatic Stability</i>			
Feeling Low Temp.	55.3 (63)	30.2 (19)	69.8 (44)
Chilled/Shivery	63.2 (72)	19.4 (14)	80.6 (58)
Hot or Cold Spells	57.0 (65)	12.3 (8)	87.7 (57)
Fever and Chills	57.0 (65)	6.2 (4)	93.8 (61)
Feeling High Temp.	50.9 (58)	1.7 (1)	98.3 (57)
<i>Pain</i>			
Abdomen Pain	49.1 (56)	21.4 (12)	78.6 (44)
Eye Pain	36.8 (42)	11.9 (5)	88.1 (37)
Chest Pain	34.2 (39)	10.3 (4)	89.7 (35)
<i>Sleep Disturbance</i>			
Difficulty falling Asleep	71.1 (81)	21.0 (17)	79.0 (64)
Difficulty staying Asleep	78.9 (90)	17.8 (16)	82.2 (74)
Need to Nap Daily	79.8 (91)	12.1 (11)	87.9 (80)
<i>Neurosensory, Perceptual & Motor</i>			
Tense Muscles	60.5 (69)	26.1 (18)	73.9 (51)
Disturbances in eyesight	43.0 (49)	16.3 (8)	83.7 (41)
Paralysis	11.4 (13)	15.4 (2)	84.6 (11)
Neck weak	54.4 (62)	14.5 (9)	85.5 (53)
Feel Unsteady on Feet	68.4 (78)	10.3 (8)	89.7 (70)
Blurred Vision	44.7 (51)	9.8 (5)	90.2 (46)
Muscle twitching	50.9 (58)	8.6 (5)	91.4 (53)
Morning Stiffness	78.9 (90)	6.8 (6)	93.2 (82)
Tingling Feeling	57.9 (66)	6.1 (4)	93.9 (62)
Legs weak	64.9 (74)	5.4 (4)	94.6 (70)
Shoulders weak	50.9 (58)	5.2 (3)	94.8 (55)
Arms weak	64.9 (74)	2.7 (2)	97.3 (72)
<i>Neuroendocrine</i>			
Weight Change	52.6 (60)	20.0 (12)	80.0 (48)
Sweating Hands	16.7 (13)	15.8 (3)	84.2 (16)
Poor Appetite	39.5 (45)	15.6 (7)	84.4 (38)
Night Sweats	38.6 (44)	9.3 (5)	90.7 (39)
<i>Mood</i>			
Anxiety/Tension	74.6 (85)	29.4 (25)	70.6 (60)
Depression	69.3 (79)	27.8 (22)	72.2 (55)
Easily irritated	69.3 (79)	15.2 (12)	84.8 (67)

Symptom	6 Months % (n)	Before Fatigue % (n)	After Fatigue % (n)
Mood Swing	46.5 (53)	13.2 (7)	86.8 (46)

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