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ABSTRACT This study examined how the mode of onset for myalgic encephalomyelitis and chronic fatigue syndrome (ME and CFS) impacts patients' presenting symptomatology. Specifically, this study investigated the differences between the most commonly reported ME and CFS onsets: infectious, stress-related, and a combined infectious and stress-related onset (referred to as 'combined onset'). Three patient samples were combined and utilized. All participants met Fukuda et al. (1994) criteria and self-reported their illness onset. Analyses showed the infectious group reported the most impairment for general health functioning—which relates to the susceptibility of getting or feeling sick—in comparison to the stress-related group. Meanwhile, both the stress-related and combined groups reported more impairment for mental health functioning than the infectious group. Lastly, the infectious and combined groups reported worse autonomic and immune symptomatology than the stress group. These findings illustrate that the mode of onset for ME and CFS could play a factor in a patient's prognosis. An infectious onset might lead to worse physical and somatic symptoms, while a stress onset might lead to worse psychological functioning. These findings are consistent with prior research. Future research should continue investigating the differences among patients based on illness onset, as well as other factors (e.g., psychiatric co-morbidity).

INTRODUCTION

Myalgic encephalomyelitis and chronic fatigue syndrome (ME and CFS) are elusive illnesses with controversial etiologies (Afari & Buchwald, 2014). While numerous case definitions exist (Carruthers et al., 2003; Carruthers et al., 2011; Fukuda et al., 1994), ME and CFS are characterized by a variety of core symptoms including profound fatigue, post-exertional malaise, impairment of memory and concentration, unrefreshing sleep, arthralgia and/or myalgia, and several autonomic, neuroendocrine, and immune manifestations (Carruthers et al., 2003). Patients often report an infectious onset, stress-related onset, or a

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combined infectious and stress-related onset (Becker, McGregor, & Meirleirxy, 2002). Within these different patient groups, various ME and CFS sub-types might exist (Jason et al., 2001). Therefore, research should examine how the symptomatology of these sub-types differs, as treatments could be tailored to patients accordingly. This study investigates how the mode of illness onset for ME and CFS affects the presenting symptomatology and functionality of patients.

An infectious onset of ME and CFS is defined by a patient having a transferrable illness (e.g. Epstein-Barr virus) prior to contracting ME or CFS. Infectious onsets have been referred to as sudden events, and people with this type of onset are more likely to attribute their illness to a physical cause (Butler, Chalder, & Wessely, 2001; Komaroff, 1988). One study found a greater likelihood for this group to be socially extraverted before their illness (Masuda, Munemoto, Yamanaka, Takei, & Tei, 2002). Research has shown physical attributions to be more often reported than psychological attributions (Butler et al., 2001; White, Lehman, Hemphill, Mandel, & Lehman, 2006). An infectious onset may also lead to worse functional impairment (Sharpe, Hawton, Seagroatt, & Pasvol, 1992), worse memory problems, (DeLuca, Johnson, Ellis, & Natelson, 1997), and a decreased likelihood of improvement over time (Vercoulen et al., 1996).

Over the years, three families of viruses—herpes viruses, enteroviruses, and retroviruses—have been studied, but identifying a single infectious, etiological agent for ME and CFS has been inconclusive (Lorusso et al., 2009). Investigators have posited that some pathophysiological anomalies may precipitate or perpetuate ME and CFS, but the illness is likely multi-faceted. An aggregate of immunological studies suggests a "hit and run" effect, where a patient contracts a virus that causes immune abnormalities, which then leads to ME and CFS; however, when the virus is eliminated, the patient's immune system remains in an activated state (Lorusso et al., 2009).While no single etiological agent has been determined, many patients attribute their illness solely to an infection, and thus, research should continue comparing their prognosis to those of patients with other onset modes.

Many patients report the development of their ME and CFS to occur after stressful life events (e.g., vehicle accident, surgery) (Becker et al., 2002; Hatcher & House, 2003; Theorell, Blomkvist, Lindh, & Evengard, 1999; Wessely et al., 1995). Although the majority of patients report an infection to play some role in their onset (Anderson, Jason, & Hlavaty, 2014; Butler et al., 2001), some patients have no clinical or laboratory evidence of viral infection (Farrar, Locke, & Kantrowitz, 1995). Hatcher and House (2003) found stressful life events—which occurred three months prior to ME and CFS—to be common. Noting these events is important, as psychological strain has been theorized to impair the Hypothalamic-Pituitary Adrenal axis (HPA-axis), which would disturb the neuroendocrinological responses in ME and CFS patients (Cleare, 2003). When the HPA-axis becomes dysregulated and over-produces cortisol and dehydroepiandrosterone, a person's immune system may weaken (Cohen, Janicki-Deverts, & Miller, 2007; Morale et al., 2001); thus, stress could prompt the development of ME and CFS.

A stress-related onset has often been reported as a gradually occurring process (DeLuca et al., 1997). Because this group is more likely to endure difficult life events, they may be more inclined to believe they played a role in causing their illness (internal attribution), which may lead to depressive symptoms (Peterson, Schwartz, & Seligman, 1981). For example, if someone ascribed their illness to work stress, they might take blame for their illness because they felt they could have reduced their work hours. However, once sick with ME and CFS, they no longer believe they have control over their symptoms (White et al., 2006). Research has suggested that people with an internal (psychological) attribution, who also have an external locus of control over their ME or CFS, will have worse psychological adjustment (White et al., 2006).

Congruent with the convoluted nature of ME and CFS, many patients attribute their illness to

a combination of infection and stress-related factors (Becker et al., 2002; Butler et al., 2001; Theorell et al., 1999). These multi-faceted onset attributions support theories that ME and CFS are heterogeneous in nature (Afari & Buchwald, 2014).

The goal of this study was to examine how the mode of ME and CFS onset impacts patients' presenting symptomatology. While other ME and CFS onset modes exist, this study investigated the differences between the most commonly reported onsets: infectious, stress-related, and a combined infectious and stress-related onset (referred to as 'combined onset'). Based on previous research, and the physical nature of an infection, we predicted that an infectious onset would result in more severe symptomatology and impaired physical functioning when compared to a stress-related onset. Conversely, we predicted that a stress-related onset would result in worse mental functioning when compared to an infectious onset. Lastly, we predicted that a combined onset would result in worse physical and mental functioning, as well as worse symptomatology, compared to the other two groups, as the two-fold effect of both an infection and stress may compound impairment.

METHODS

PARTICIPANTS

Three patient samples were combined and utilized: the *DePaul sample*, the *Norway sample*, and the *Newcastle-uponTyne Royal Victoria Infirmary sample*. Case ascertainment methods differed between the samples. Participants in the *DePaul sample* were adults who self-identified as having CFS, ME/CFS, or ME; participants in the *Norway sample* were diagnosed with CFS by a physician or medical specialist, or came from an inpatient medical ward for severely ill patients, or were from an outpatient clinic; and participants in the *Newcastle-uponTyne Royal Victoria Infirmary sample* were recruited from a primary care setting, after completing a medical workup. All participants had to meet the Fukuda et al. (1994) criteria to be included in the present study.

DePaul Sample

Eligibility for inclusion was met with the following criteria: an individual needed to be (a) between the ages of 18 and 65; (b) literate in English; (c) and have a self-reported current diagnosis of CFS, ME/CFS, or ME. Recruitment occurred in a variety of settings, including posts on internet forums, contacting support groups, and following up with individuals who previously participated in a DePaul study while expressing interest in future studies. In addition, individuals who had emailed the team with interest in future studies were contacted. Three options were available for survey completion: an electronic survey, a hard-copy survey, or a verbal survey over the telephone. Surveys could be completed either at home or in-person at DePaul University's Center for Community Research. Five-dollar Amazon.com gift cards were given to the first 100 individuals who completed the survey.

Norway Sample

This sample consisted of patients from four mid-sized towns in southern Norway, as well as an inpatient medical ward and an outpatient clinic at a multidisciplinary CFS/ME center. Recruitment occurred through healthcare professionals, a waiting list for a patient education program, and CFS patient organizations. Participants needed to be between 18 and 65 years old and be literate in Norwegian. Before participants could be included in the sample, they had to complete a written informed consent process.

Newcastle Sample

This sample consisted of participants who were suspected of having CFS by primary care physicians after a complete medical assessment at the Newcastle-upon-Tyne Royal Victoria clinic. At the clinic, an experienced consultant physician collected a comprehensive medical history and examined each individual. 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.

MEASURES

Medical Outcomes Study 36-item Short-Form Health Survey (SF-36 or RAND-36)

All participants completed the SF-36. This 36-item measure allows participants to self-report their functional and mental health status. Scores on 100-point scales are calculated for the following domains: physical functioning, role physical (a measure of the impact of physical health problems on ability to fulfill life roles), bodily pain, general health (a measure of global perceptions of overall health), social functioning, mental health functioning, role emotional (a measure of the impact of mental health problems on ability to fulfill life roles), and vitality (a measure of fatigue/energy). Higher scores indicate better health or less impact of health on functioning. On this form, an example question reads: *How true or false is each of the following statements for you? I expect my health to get worse (Definitely true; Mostly true; Don't know; Mostly false; Definitely false)*. Studies assessing the SF-36 construction have found adequate internal consistency, significant discriminant validity among subscales, and substantial differences in the pattern of scores between patient and non-patient populations (McHorney, War Jr, Lu, & Sherbourne, 1994).

The DePaul Symptom Questionnaire (DSQ)

All participants also completed the DSQ (Jason et al., 2010). This measure allows participants to self-report their illness onset, symptomatology, demographics, and medical, occupational, and social history. On a five-point Likert-scale, participants rated the frequency and severity of 54 symptoms over the past six months. For frequency, the items state "Throughout the past 6 months, how often have you had this symptom?" (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). For severity, the items state "Throughout the past 6 months, how much has this symptom bothered you?" (0 = symptom not present, 1 = mild, 2 = moderate, 3= severe, and 4 = very severe). Frequency and severity scores were each multiplied by 25 to create 100-point scales. The 100-point frequency and severity scores for each symptom were then averaged to create one score per symptom. The development of the DSQ was based upon the Clinical Canadian Criteria (Carruthers et al., 2003), which identifies seven symptom domains (fatigue/post-exertional malaise, neurological dysfunction, sleep dysfunction, pain, autonomic dysfunction, immune dysfunction, and neuroendocrine dysfunction). Thus, DSQ symptom scores are grouped by these seven theoretical domains for analysis. Among both patient and control groups, the DSQ has illustrated good test-retest reliability (Jason, So, Brown, Sunnquist, & Evans, 2015) with factors evidencing good internal consistency (Brown & Jason, 2014).

ANALYSIS

Participants were divided into one of three onset groups—infectious, stress, or combined infectious and stress—based on their responses to the DSQ item: *Did your fatigue/energy related illness start after you experienced any of the following? (Check one or more and please specify): An infectious illness, An accident, A trip or vacation, An immunization (a shot at doctor's office), Surgery, Severe stress (bad or unhappy events), Other (please list), I am not ill.*

Although participants could have marked more than one answer to the DSQ onset item, they were only included in this study if they reported an infectious, stress, or combined infectious and stress onset. For instance, if a participant reported an infectious onset and an onset after a trip or vacation, they would be assigned to the infectious-only group. Similarly, if a participant reported a stress onset and an onset after a trip or vacation, they would be assigned to the stress-only group. The infectious, stress, and combined infectious and stress onset groups are the most likely precipitating factors of ME and CFS (Becker et al., 2002), while events like an accident, trip or vacation, an immunization, or surgery might precipitate an infection or cause stress (e.g., someone contracts an infection while on a trip). If, however, a participant reported having an infectious and stress onset, they were assigned to the combined group. A multivariate

analysis of variance (MANOVA) was used to compare these three groups on symptomatology and the SF-36 subscales, followed up by univariate and post-hoc comparisons when indicated. An alpha level of .05 was used for all statistical tests.

RESULTS

SAMPLES

The combined sample (DePaul, Newcastle, and Norway) consisted of 495 participants. However, 101 of these participants were excluded because they did not endorse either an infectious or stress onset; four of these excluded participants endorsed "onset after an accident," four endorsed "after a trip or vacation," 11 endorsed "after an immunization," 17 endorsed "after surgery," and 56 selected "other." After these exclusions, the combined sample was 394 participants; 151 were included from the DePaul sample, 60 were included from the Newcastle sample, and 183 were included from the Norway sample. These three groups were not significantly different on mode of illness onset, ethnicity or gender. However, there were significant differences between the samples on age [$F(2, 372) = 22.67$, $p<.001$], education level [$X^2(15, 389) = 178.50$, $p<.001$], and work status [$X^2(12, 373) = 167.14$, $p<.05$].

The DePaul sample was significantly older than the other two samples with a mean age of 51.8, compared to the Newcastle sample with a mean of 45.9, and the Norway sample with a mean of 42.4. Regarding educational level achieved, the DePaul sample was the most educated, followed by the Newcastle sample, and then the Norway sample (80%, 53.45%, and 49.17% completed at least a standard college degree). Regarding work status, a greater percentage of the DePaul sample was unemployed compared to the Norway sample, and a greater percentage of the Norway sample was on disability compared to the DePaul sample.

Table 1 provides demographic information for the three onset groups: 213 individuals were categorized as "infectious onset," 59 individuals were categorized as "stress onset," and 122 individuals were categorized as "combined infectious and stress onset." Statistical analyses showed only one significant difference between the groups. A chi-squared test found participants with a stress-related onset were more likely to report having children compared to the infectious and combined groups, $X^2(2, 391)=9.818$, $p=.007$. The vast majority of participants in each group were female, white, and on disability.

FUNCTIONAL STATUS

Table 2 displays the SF-36 data. A multivariate analysis of variance (MANOVA) found that the three groups differed overall on these subscales [Wilks' Lamda = .894, $F(16, 728)=2.632$, $p<.001$]. The univariate tests revealed a significant overall difference on general health functioning [$F(2, 374)=3.982$, $p=.019$], mental health functioning [$F(2, 374)=8.55$, $p<.001$], and role emotional functioning [$F(2, 374)=6.247$, $p=.002$]. There was a minor violation for homogeneity of between-group variance on the Role Emotional scale, but Brown-Forsythe F and Welch's F adjustments showed that this had no impact on the observed outcome. The other subscales were non-significant. Bonferroni post-hocs revealed that the infectious group had significantly worse general health than the stress group ($p=.019$). The combined group neared significance ($p=.061$), reporting worse general health functioning than the stress-related group.

The infectious group had significantly better mental health functioning than both the stress-related ($p=.004$) and combined groups ($p=.002$). Additionally, a Games-Howell post-hoc test was conducted on the Role Emotional subscale, as this category did not meet the homogeneity of variance assumption. This test found that the combined group reported the worst functioning on the role emotional scale, but was only significantly worse than the infectious group ($p = .004$).

Table 1. Demographics (*N*= 394)

	Infectious (*n*=213)	Stress (*n*=59)	Combined (*n*=122)	
	M (SD)	*M (SD)*	*M (SD)*	
Age	46.88 (14.20)	47.53 (10.79)	46.19 (11.92)	
	% (*n*)	% (*n*)	% (*n*)	*p*
Sex				.801
Male	16.4 (35)	12.1 (7)	17.2 (21)	
Female	83.6 (178)	87.9 (51)	82.8 (101)	
Race				.661
White	97.6 (206)	98.3 (58)	99.2 (121)	
Asian/Pacific Islander	0.5 (1)	1.7 (1)	0	
Other	1.9 (4)	0	.8 (1)	
Education				.426
Less than high school	5.7 (12)	5.2 (3)	3.3 (4)	
Some high school	2.4 (5)	0 (0)	0.8 (1)	
HS degree or GED	21.3 (45)	24.1 (14)	25.8 (31)	
Partial college	9.0 (19)	13.8 (8)	5.8 (7)	
Standard college degree	35.5 (75)	39.7 (23)	36.7 (44)	
Graduate degree	26.1 (55)	17.2 (10)	27.5 (33)	
Marital Status				.758
Married/partnered	55.5 (116)	55.9 (33)	51.3 (61)	
Separated	.5 (1)	1.7 (1)	1.7 (2)	
Widowed	1 (2)	0 (0)	1.7 (2)	
Divorced	12.4 (26)	18.6 (11)	13.4 (16)	
Never Married	30.6 (64)	23.7 (14)	31.9 (38)	
Children				.007
Yes	46.4 (98)	69.5 (41)	52.1 (63)	
No	53.6 (113)	30.5 (18)	47.9 (58)	
Work Status				.134
On disability	59.7 (120)	67.3 (37)	64.1 (75)	
Student	5.0 (10)	0 (0)	2.6 (3)	
Homemaker	2.0 (4)	1.8 (1)	4.3 (5)	
Retired	10.4 (21)	7.3 (4)	6 (7)	
Unemployed	7.5 (15)	0 (0)	7.7 (9)	
Working part-time	9 (19)	16.4 (9)	13.7 (16)	
Working full-time	6 (12)	7.3 (4)	1.7 (2)	

In summary, the infectious group showed the worst general health functioning, but the highest mental health functioning compared to the other groups. On the contrary, the stress-related and combined group reported the worst mental health functioning. Additionally, the combined group showed comparable general health functioning to the infectious group; however, this finding should be taken with caution as it was not statistically significant. Lastly, the combined group reported the worst role emotional scores.

Table 2. Differences in functioning (SF-36 subscales) across modes of illness onset (N = 374)

	Infectious (n=201)	Stress (n=57)	Combined (n=116)	p
	M (SD)	*M (SD)*	*M (SD)*	
Physical Functioning	36.25 (23.49)	42.10 (19.45)	37.05 (22.67)	.223
Role Physical	7.42 (20.03)	5.70 (18.30)	4.53 (12.60)	.366
Bodily Pain	40.12 (22.83)	34.71 (21.63)	40.21 (23.48)	.256
General Health	26.87 (15.61)[a]	33.61 (17.42)[a]	27.54 (16.36)	.019
Social Functioning	25.50 (23.01)	27.85 (21.39)	22.61 (22.45)	.764
Mental Health	74.02 (16.45)[ab]	65.84 (18.14)[a]	67.36 (16.87)[b]	<.001
Role Emotional	82.59 (34.81)[a]	71.93 (41.21)	67.24 (43.07)[a]	.002
Vitality	18.18 (15.86)	19.36 (15.61)	16.89 (15.21)	.578

[ab] Similar letters note significant differences

SYMPTOMATOLOGY

Based on the symptom categories of the Clinical Canadian Criteria (Carruthers et al., 2003), the symptoms were categorized into the following domains for analysis: Fatigue/Post-Exertional Malaise (six symptoms), Sleep (six symptoms), Pain (seven symptoms), Neurological (13 symptoms), Autonomic (seven symptoms), Neuroendocrine (ten symptoms), and Immune (five symptoms). MANOVA was used to compare the three groups on the unique collection of symptoms from each of the seven theoretical symptom domains of the DSQ. The three groups were significantly different on the Autonomic [Wilks' Lambda=.93, F(2, 367)=1.904, p=.023] and Immune domains [Wilks' Lamda= .947, F(2, 359)=1.943, p=.037]. However, the Fatigue/Post- Exertional Malaise, Sleep, Pain, Neurological, and Neuroendocrine domains were non-significant.

Table 3 displays the Autonomic symptoms. The univariate tests revealed a significant difference between the groups for nausea [F(2, 370)=4.093, p=.017] and irregular heartbeats [F(2, 370)=4.949, p=.008]. Bonferroni post-hoc tests found the infectious and combined groups experienced worse nausea and irregular heartbeats than the stress group. The items dizziness or fainting [F(2, 370)=2.976, p=.052] and unsteady on one's feet [F(2, 370)=2.595, p=.076] approached significance.

Table 4 presents the Immune items. Univariate tests revealed a significant difference between the groups for sensitivity to smells/foods, etc. [F(2, 359)=3.482, p=.032] and flu-like symptoms [F(2, 359)=4.452, p=.012]. Bonferroni post-hoc tests found the combined group to experience

Table 3. Differences in autonomic symptoms across modes of illness onset (N=370)

	Infectious (n=198)	Stress (n=53)	Combined (n=119)	p
	M (SD)	*M (SD)*	*M (SD)*	
Bladder problems	27.90 (30.24)	33.73 (38.10)	29.90 (32.72)	.418
Irritable bowel problems	47.16 (31.72)	46.70 (33.72)	52.84 (34.84)	.291
Nausea	36.93 (26.81)[a]	25.71 (23.18)[ab]	37.50 (28.79)[b]	.017
Unsteady on your feet	43.24 (28.40)	33.73 (25.31)	39.81 (27.18)	.076
Shortness of breath	41.22 (28.10)	34.67 (31.26)	40.91 (28.34)	.317
Dizziness or fainting	42.42 (27.73)	32.78 (24.42)	42.33 (25.37)	.052
Irregular heartbeats	33.84 (28.21)[a]	23.35 (23.52)[ab]	37.92 (29.65)[b]	.008

[ab] Similar letters note significant differences

Table 4. Differences in immune symptoms across modes of illness onset (*N*=359)

	Infectious (*n*=194)	Stress (*n*=51)	Combined (*n*=114)	*p*
	M (SD)	*M (SD)*	*M (SD)*	
Sore throat	39.82 (27.55)	35.04 (23.32)	41.78 (27.47)	.335
Lymph nodes	40.08 (30.35)	32.84 (28.61)	35.42 (27.47)	.198
Fever	20.72 (24.50)	20.10 (23.19)	19.96 (23.74)	.961
Flu-like symptoms	56.96 (25.76)[a]	47.06 (26.53)[ab]	60.09 (26.39)[b]	.012
Sensitivity to smells/foods/ medications/ chemicals	44.39 (36.10)	35.05 (35.88)[a]	50.82 (35.60)[a]	.032

[ab] Similar letters note significant differences

significantly worse sensitivity problems compared to the stress group, but not the infectious group. Both the infectious and combined group reported significantly worse flu-like symptoms compared to the stress group.

DISCUSSION

This study adds to the literature of predicting the prognosis of ME and CFS based upon knowledge of illness onset. Previous work has shown that illness attribution (physical vs. psychological), illness duration, an internalization of symptoms, a psychiatric co-morbidity, and stressful life events play a role in a patient's outcome. Given these findings, we hypothesized that an infectious onset would lead to different levels of symptom impairment compared to a stress-related onset. Specifically, we predicted that an infectious onset would lead to worse physical well-being and symptomatology, while a stress-related onset would lead to worse mental well-being. Further, we predicted that a combined infectious and stress-related onset would compound symptomatology, perhaps limiting one's ability to cope, resulting in the worst impairment for both physical and mental well-being, and more severe symptomatology.

The findings lend some support to these hypotheses. Analyses showed the infectious group reported the most impairment for general health functioning—which relates to the susceptibility of getting or feeling sick (e.g. "I seem to get sick more than most people")—in comparison to the stress-related group. This data is congruous with the notion that people with an infectious onset could still be suffering from the ramifications of a virus or bacterium (Lorusso et al., 2009). Although not statistically significant from the other two groups, the combined group also reported impairment for general health functioning

The data also support our hypothesis that a stress-related and combined onset would result in worse mental well-being compared to an infectious onset. For the mental health subscale, both the stress-related and combined groups reported more impairment than the infectious group. This data corroborates prior research that stressful life events and the internalization of symptoms may hamper one's ability to psychologically cope. However, only the combined group experienced more impairment on the role emotional subscale compared to the infectious group; this finding also supports our hypothesis that the combined group would report the worst overall impairment in mental well-being. These findings suggest that the two-fold factor of contracting an infection—and experiencing life stress—could increase the risk for emotional impairment over time

Furthermore, we found differences between these onset groups within the autonomic and immune symptom domains. As predicted, the infectious and combined groups reported worse

autonomic and immune symptomatology than the stress group. Nausea, irregular heartbeats, and flu-like symptoms were found to be significantly worse in the infectious and combined groups; the combined group also had worse sensitivity to smells/foods/medications/chemicals than the stress group. Although non-significant, the infectious and combined groups reported worse impairment for the dizziness or fainting symptom. Because this symptom relates to general health functioning (e.g. feeling sick), and may co-occur with an infection, researchers and physicians should be cognizant that this symptom could be worse—or more prevalent—in patients with an infectious onset. Taken as a whole, these results support the speculation that patients with an infectious onset could be affected by an overactive immune system (Lorusso et al., 2009).

These findings illustrate that the mode of onset for ME and CFS could play a factor in a patient's prognosis. An infectious onset might lead to worse physical and somatic symptoms, while a stress onset might lead to worse psychological functioning. Therefore, both physicians and researchers should make note of illness onset when working with patients. The field's focus on psychological factors has frustrated many patients with ME and CFS. Patients with ME and CFS have commonly expressed dissatisfaction with their physicians regarding stigma and inadequate treatment (Åsbring & Närvänen, 2002; Dickson, Knussen, & Flowers, 2007). In the past, patients have reproached physicians for not believing ME and CFS to be an organic illness (Deale & Wessely, 2001). Therefore, tailoring treatments for this diverse patient population is of great importance.

The present study's limitations must also be noted. We did not apply psychiatric exclusions when determining which participants to include in the present study. A comorbid psychiatric illness might impact a participant's functioning and illness experience, and we were unable to account for this when comparing onset groups. A second limitation is the method of classifying patients into the three onset groups. Although patients could have reported multiple types of onset, we categorized only into an infectious onset, stress-related onset, and a combined onset. For instance, a participant who listed both *infectious onset* and *got their illness after vacation* would be sorted into the infectious group. This decision was made based on the previous research, as these three onsets appear to be the most commonly endorsed triggers for the illness (Afari & Buchwald, 2014; Becker et al., 2002; White et al., 2006). Furthermore, the other onsets (e.g. an accident, trip or vacation, immunization, surgery) may commonly co-occur with an infectious or stress onset. For instance, a patient might have had surgery, experienced stress because of the surgery, and then contracted ME and CFS.

Additionally, the present study included participants from three unique samples that were recruited differently and had both demographic similarities and differences. The resulting combined sample was thus not homogeneous, and it may be more appropriate to study subsamples of patients stratified by case ascertainment method in the future. We selected to combine these groups to allow for greater statistical power in our subsequent analyses. Notably, when participants were categorized into the three onset groups, the resulting groups were comparable on almost all demographic outcomes. Additionally, our distribution of the three illness onset groups is consistent with other research samples (Becker et al., 2002; Salit, 1997; White et al., 2006). About 68% of our sample believed an infection played some role in their onset, and 37% believed stress played some role. White and colleagues (2006) found 61% of their sample attributed their illness to either a flu, virus, bacteria, or infection, and 43% attributed their illness to either stress, overwork, or over activity. Becker and colleagues (2002) also identified infections to be combined with non-infectious stressors, such as psychological stress, in the onset of ME and CFS. Finally, this study relied on self-report data, and thus, there was no outside, objective documentation of the participants' illness onset.

Over the years, findings regarding the onset of ME and CFS and subsequent functioning and symptomatology have been equivocal, and the

illness experiences amongst patients have been variable. However, by investigating ME and CFS onset, we may gain a better understanding of a patient's illness progression, which may inform the development and implementation of treatments. The findings of this study corroborate prior research. Future research should continue investigating the differences among patients based on illness onset, as well as other factors (e.g., psychiatric co-morbidity).

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