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Deconstructing post-exertional malaise: An exploratory factor analysis

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Abstract

Post-exertional malaise (PEM) is a cardinal symptom of myalgic encephalomyelitis (ME) and chronic fatigue syndrome (CFS). There are two differing focuses when defining PEM: a generalized, full-body fatigue and a muscle-specific fatigue. This study aimed to discern whether PEM is a unified construct or if it is composed of two smaller constructs, muscle fatigue and generalized fatigue. An exploratory factor analysis was conducted on several symptoms that assess PEM. The results suggest that PEM is composed of two empirically different experiences, one for generalized fatigue and one for muscle-specific fatigue.

Keywords

Myalgic encephalomyelitis; chronic fatigue syndrome; post-exertional malaise; operationalization; factor analysis

Introduction

One of the primary symptoms of chronic fatigue syndrome (CFS) and myalgic encephalomyelitis (ME) is post-exertional malaise (PEM). This symptom has been used to differentiate patients from healthy controls and exclusionary conditions such as depression (Jason et al., 2015b; Hawk et al., 2006). PEM is often measured using various objective and subjective measures.

Submaximal and maximal exercise tests have been used to objectively indicate the presence of PEM. Maximal tests often require patients to participate in an exercise test until they reach a peak respiratory exchange ratio or cross the anaerobic threshold for oxygen consumption, which is often done within 5–10 minutes (Noonan and Dean, 2000; Cook et al., 2006). These tests can demonstrate PEM, especially over a two-day period as it can take 24 hours for symptoms to appear (Van Ness et al., 2007). Alternatively, submaximal exercise tests predict aerobic capacity by asking participants to maintain a level of effort for a certain amount of time, often much longer than maximal tests (Light et al., 2011). Additionally, these tests often involve the collection of blood samples to examine different biomarkers, and these tests may also not be available to many patients. However, the nature of these exercise tests requires the patients to exert themselves, thus possibly exacerbating existing

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PEM or causing PEM. Additionally, these types of tests require an expert that is familiar with the methodology and interpretation of the findings. As a result, self-report, subjective data are often used to assess the presence and severity of PEM (Jason et al., 1999).

Due to ambiguity in operationalizing case definition criteria, PEM symptoms have been measured using a variety of self-assessment instruments. The DePaul Symptom Questionnaire (DSQ) is one self-report measure of symptomatology for ME and CFS (Jason et al., 2010). This questionnaire was derived from the Canadian ME and CFS case definition (Carruthers et al., 2003) and assesses the frequency and severity of 54 symptoms. A factor analysis by Jason et al. (2015d) determined six symptoms constitute a distinct PEM construct: fatigue/extreme tiredness; dead, heavy feeling after starting to exercise; mentally tired after the slightest effort; minimum exercise makes physically tired; next day soreness after non-strenuous, everyday activities; and physically drained or sick after mild activity. The DSQ has evidenced good test-retest reliability for both patients and control groups (Jason et al., 2015c). The ME International Consensus Criteria (ME-ICC; Carruthers et al., 2011) has also provided self-report questions to assess the construct of PEM (referred to as post-exertional neuroimmune exhaustion, or PENE) in their primer: marked, rapid physical or cognitive fatigability in response to exertion; post-exertional exhaustion that may be immediate or delayed; exhaustion that is not relieved by rest; symptoms that worsen with exertion; and substantial reduction in pre-illness activity level due to low threshold physical and mental fatigability.

With the variety of questions utilized to assess PEM, how a question is phrased is also of importance, as different phrasing can illicit varying responses. However, many patients attempt to reduce the frequency and severity of their PEM by pacing themselves and staying within their energy limits (Jason et al., 2008). As a result, they may not be currently experiencing PEM. This, in turn, could impact the way patients respond to certain subjective questions. Jason et al. (2015a) found that 25% of participants would respond “no” to the question, “Do you feel generally worse than usual or fatigued for 24 hours or more after you have exercised?” Yet, of those that answered “no”, all of them answered “yes” to the question, “Do you experience high levels of fatigue or weakness following normal daily activity?” This finding indicated that the specificity of the first question, requiring 24 hours of fatigue and mentioning exercise, resulted in many patients not being counted as having PEM. Additionally, Jason et al. (1999) noted that the endorsement of PEM ranged from 40.6–93.8% of a group of individuals, depending on how the question was phrased.

However, there is disagreement over what constitutes post-exertional malaise. Holmes et al. (1988) considered this symptom to be a prolonged generalized fatigue after exercise levels that would not have evoked this profound fatigue in the premorbid state. Carruthers et al. (2011) state that PEM is more than just generalized fatigue, as they refer to it as an abnormal exacerbation of symptoms following exertion. Ramsay (1988) described it as muscle fatigue after exercise in which power for the affected muscles is not fully restored for three or more days. Hyde (2007) defined PEM as a rapid loss of muscle strength after moderate mental or physical activity. Additionally, Goudsmit et al. (2009) defined the symptom as abnormal level of muscle fatigue as a result of minor activity levels, which exacerbates over 48 hours. As such, some descriptions of PEM emphasize musculoskeletal fatigue, while others refer to

PEM as a more generalized exacerbation of the entire symptom complex. Therefore, it may be beneficial to include a variety of questions that assess both musculoskeletal and generalized fatigue to accurately reflect the experience of PEM among the patient population.

The purpose of this study was to investigate the characteristics of the symptom referred to as post-exertional malaise. An exploratory factor analysis was utilized to determine if PEM represents one entity or if there are empirically different experiences of PEM. It was hypothesized that the results would indicate the presence of two separate constructs; one that assesses muscle-related fatigue, and one that assesses a generalized fatigue and exacerbation of symptoms. It is hoped that the findings of this study will help clarify the operationalization of this cardinal ME and CFS symptom, thus leading to an improvement in diagnostic reliability.

Methods

Measures

Participants completed a series of questionnaires to assess the frequency and severity of their CFS and ME symptoms. Seventeen questions that measured PEM were selected from the DePaul Symptom Questionnaire (Jason et al., 2010), Ramsay's clinical description of ME (Ramsay, 1988), the Jason et al. (1997) CFS screening study, the ME-ICC (Carruthers et al., 2011), the Chalder Fatigue Scale (Chalder et al., 1993), and the Medical Questionnaire (Komaroff and Buchwald, 1991). The questions and their sources are listed in Table 1. Items were phrased with specific verbiage to assess the frequency and severity of PEM over the past six months. A prior study by Evans & Jason (2013) suggested that this six-month timeframe led to the most reliable reports of PEM and other CFS symptoms. Participants rated each PEM symptom's frequency for the past six months on a 5-point Likert scale: 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. Similarly, participants also rated each PEM symptom's severity for the past six months on a 5-point Likert scale: 0=symptom not present, 1=mild, 2=moderate, 3=severe, 4=very severe. These scores were used to create a composite score for each symptom. The frequency and severity were converted to a 100-point scale by multiplying each one by 25 and then averaging them for each individual question. The six items from the DSQ have previously been tested on this frequency and severity scale and have shown good test-retest reliability (Jason et al., 2015c). However, the remaining eleven items have not been previously tested on this frequency and severity scale.

Additionally, participants completed the Bell Ability Scale (Bell, 1994) and the SF-36 Physical Functioning subscale (Ware et al., 2000). The SF-36 is a self-report disability measure. The participants answered questions on a 3-point Likert scale, which was then converted to a 100-point scale. This measure has shown good discriminant validity and internal consistency (McHorney et al., 1993). Similarly, the Bell Ability Scale is a 10-point scale that measures a patient's physical functioning. Patients were given a list of functional status examples (e.g. unable to care for self) and they selected the number that best fit their current physical functioning. This scale was adapted to a 100-point scale to allow for more

variability in scores if the participant felt their functioning was between two examples. Both of these measures were utilized to gauge a participant's current functioning level.

Research Sample

An international convenience sample was collected of adult patients self-identifying as having ME or CFS. Participants needed to be able to read and write English and have a current, self-reported diagnosis of ME or CFS. Individuals were recruited from several sources: newsletters of patient organizations, social media, and internet forums. Participants completed the study measures online using Research Electronic Data Capture (REDCap), an online survey tool (Harris et al., 2009). Participants were able to save their answers and return to complete the survey at a later time if they were not able to finish it all at once. There was no timeline for completing the questionnaire as the illness can lead to unpredictable, rapid declines in functioning on any given day.

The sample ($N = 704$) was predominantly female with just 10.3% male participants. Most participants were Caucasian (96.4%), and only 2% identified themselves as being of Latino or Hispanic origin. For marital status, 56.4% were married or living with a partner, 2.6% were separated, 1.1% widowed, 13.4% divorced, and 26.5% never married. For education, 10.6% completed high school or less; 22.8% had at least one year of college; 33.7% had college degree; and the remaining 32.9% had a graduate or professional degree. Regarding work status, 42.2% were on disability; 3.0% were students; 4.9% were homemakers; 10.5% were retired; 16.8% were unemployed; 15.8% worked part-time; and the remaining 6.8% worked full-time. More than half of the participants, 54.8%, reported currently living outside of the United States.

Results

Factor Analysis

Assessing the adequacy of the correlation matrix—Before running the exploratory factor analysis (EFA) on the sample, the adequacy of the correlation matrix was assessed. There were no pairs of items that were highly correlated (>0.8), demonstrating that multicollinearity was not a potential issue. Bartlett's test of sphericity indicated the correlation matrix was not an identity matrix ($X^2 = 8225.84$, $p < 0.001$). The Kaiser-Meyer-Olkin measure of sampling adequacy ($KMO = 0.96$) also indicated the matrix was appropriate for EFA. Finally, measures of communality for all items were $>.60$, which indicated that EFA was appropriate.

Factor extraction and determining the number of factors to be retained—Fifty-four participants were excluded from the factor analysis due to incomplete data. Principal axis factoring was used with an oblique rotation (promax). An examination of eigenvalues (greater than one) and the scree plot suggested a two-factor solution; only two factors had eigenvalues >1 .

Factor Interpretation—Table 1 shows the factor pattern matrix for the solution. Twelve items loaded on Factor I and five items loaded on Factor II. No items were dropped from the

analysis due to loadings < 0.4 . Factor I was labeled the General factor, as the items that loaded tended to assess a general exacerbation of the symptom complex including fatigue. Factor II was labeled the Muscle factor, as these items assess fatigue of the musculoskeletal system. The two factors were strongly correlated, $r = 0.754$. Additionally, Cronbach's alpha was computed for each factor. Cronbach's alpha for Factor I ($\alpha = .944$) and Factor II ($\alpha = .873$) items indicated that both factors possess good internal consistency. To compute factor scores, the regression method was used.

Factor Scores—Table 2 presents the correlations and overall mean factor score differences for demographic variables within each factor. As the table shows, the General factor scores were negatively correlated with the SF-36 Physical Functioning subscale, $r = -.612$, and the Bell Ability Scale, $r = -.643$ (all $ps < .001$). Similarly, the Muscle factor scores were negatively correlated with the SF-36 Physical Functioning subscale, $r = -.610$, and the Bell Ability Scale, $r = -.560$ (all $ps < .001$). These findings indicate that more frequent and severe symptoms are associated with worse functioning.

Factor scores also significantly differed across various demographic categories. There was a significant effect of marital status on General factor scores [$F(2,642) = 4.45, p < .05$] and Muscle factor scores [$F(2,642) = 3.66, p < .05$]. Games-Howell post-hoc tests showed that individuals who were married had significantly lower scores, meaning less perceived impairment, than those who were separated, divorced, or widowed, $p < .05$.

Additionally, there was a significant effect of current income on General factor scores [$F(4,540) = 3.52, p < .01$] and Muscle factor scores [$F(4,540) = 5.56, p < .001$]. Post-hoc analyses were not computed due to small sample sizes in the higher income categories, though scores decreased as income increased.

Work status was significantly related to the Muscle factor scores, $F(6,633) = 14.00, p < .001$. A Games-Howell post-hoc test showed that individuals who were working part-time had significantly lower scores than participants who indicated they were on disability, a student, homemaker, retired, or unemployed (all $ps < .05$). Additionally, individuals who were working full time had significantly lower mean factor scores compared to those who indicated they were on disability or unemployed, $p < .05$. For the General factor, a Welch's F test was used due to violating the assumption of homogeneity of variance; results indicated significant differences in work status, $F(6, 121.65) = 14.41, p < .001$. Games-Howell post-hoc tests revealed similar results to those of the Muscle factor analysis. Those working part-time had significantly lower scores than those who were on disability, homemakers, retired, or unemployed (all $ps < .05$). Those working full-time had significantly lower scores than those who were unemployed or on disability, $p < .001$.

Finally, there was a significant effect of education level on General factor scores, $F(3,639) = 3.79, p < .01$. A Games-Howell post-hoc test showed that individuals with a standard college degree had lower scores than those with a high school degree or less, $p < .05$. For the Muscle factor, a Welch's F test was used due to violating the assumption of homogeneity of variance; results indicated a significant difference, $F(3, 263.96) = 8.75, p < .001$. Games-Howell tests revealed similar results to those of the General factor analysis. Those with a

standard college or graduate degree had significantly lower scores than those who completed partial college or less, $p < .01$.

Symptom Presence

A symptom was determined to be present if it was present for at least half of the time (frequency ≥ 2) with moderate severity (severity ≥ 2) over the past six months (a 2-2 threshold). Table 3 shows the percentage and number of participants that have each symptom at the required threshold. Almost all of the participants, 99.6%, had at least one of the PEM symptoms. Additionally, 94.9% had at least one symptom from the Muscle factor and 99.3% had at least one symptom from the General factor. For the participants that did not meet at least one item in the Muscle factor, the functioning level was significantly higher than those that did meet one item in both the Bell Ability Scale [$F(1,591) = 39.16, p < .001$] and the SF-36 Physical Functioning subscale [$F(1,591) = 35.57, p < .001$]. Additionally, 47.2% of those that did not meet at least one muscle symptom were able to work at least part-time compared to 21.2% of the participants that did have at least one muscle symptom present at the 2-2 level. A Fisher's Exact Test showed that the group that did not meet any Muscle factor symptoms were significantly more likely to work at least part-time, $p < .001$.

The five PEM items taken from the DePaul Symptom Questionnaire (Jason et al., 2010) captured 97.0% of the sample. Those items are: next day soreness or fatigue after non-strenuous, everyday activities; dead, heavy feeling after starting to exercise; minimum exercise makes you physically tired; physically drained or sick after mild activity; and mentally tired after the slightest effort. These symptoms encompass items that were loaded into both the General and the Muscle factors.

Discussion

An exploratory factor analysis was conducted on several self-report items that are commonly used to assess the presence of PEM in patients with ME and CFS. The purpose was to determine if the construct referred to as PEM is a unified entity or if it can be separated into entities that assess different experiences of PEM. The findings propose a two-factor solution: a General factor and a Muscle factor. Additionally, differences in factor scores across demographic variables were assessed to determine whether certain demographic attributes might influence PEM severity.

The EFA indicated a two-factor solution with one factor focusing on generalized symptom complex exacerbation and the other focusing on musculoskeletal system fatigue. The General factor was composed of 12 PEM symptoms related to a generalized feeling of physical or mental fatigue following exertion. The Muscle factor was composed of five symptoms that referred to pain, weakness, or fatigue in muscles following exertion. This finding indicates that PEM is composed of two distinct constructs that may warrant separate assessment during diagnosis. As shown in Table 3, 94.9% of patients have at least one symptom that occurs at least half of the time and at moderate severity (the 2-2 threshold) in the Muscle factor and 99.3% of patients have at least one symptom in the General factor. The 5.1% of participants that did not meet any symptoms in the Muscle factor had significantly better functioning levels and were more likely to work part-time or full-time.

This finding suggests that there may be a subgroup of ME and CFS patients that are less impaired than the rest of the patient population. Additionally, it is important to note that although the results indicate two distinct constructs within PEM, the majority of participants are experiencing symptoms in both the Muscle and the General factors.

Further research should determine the combination of symptoms from each factor that would capture the most patients. Interestingly, the DSQ (Jason et al, 2010) includes two PEM items that loaded into the Muscle factor and four that loaded onto the General factor. Thus, the DSQ assesses both experiences of PEM. The majority of patients, 89.3%, have at least one symptom at the 2-2 level in each factor when only using the DSQ questions. However, the ME-ICC (Carruthers et al., 2011) criteria includes only symptoms that load onto the General factor. Almost all of the patients, 96.3%, have at least one of the ME-ICC PEM symptoms at the 2-2 level in the General factor; however, the Muscle factor is not assessed with this criteria. Thus, any PEM experience that includes muscle-specific fatigue may not be assessed with the symptoms described in the International Consensus Primer for Medical Practitioners for this case definition (Carruthers et al., 2012).

Additionally, several significant differences were found when analyzing the association between factor scores and level of functioning. There were significant negative correlations between both factors scores and the SF-36 Physical Functioning subscale and the Bell Ability Scale. These results indicate that, as expected, more frequent and severe symptoms are associated with worse functioning.

Interestingly, there were significant differences in mean factor scores when examining marital status, education level, current work status, and household income. The scores for the individuals who can work outside the home were lower, indicating less impairment, than those of individuals who were unemployed or on disability. This finding suggests that as symptoms become more frequent and severe, the ability to work outside of the home declines. Similarly, this could explain the differences found between the patients with college degrees and the patients that completed high school or less. Bakken et al. (2014) found two age peaks in the incidence of ME and CFS in a Norwegian population, 10–19 years and 30–39 years. For individuals that developed ME or CFS during the earlier peak, the severity of the illness may have prevented some patients from completing a higher education.

There was a general trend of mean factor scores decreasing as income levels increase for both factors, which may have several possible explanations. First, patients with higher household incomes may be able to find specialized treatment for their symptoms. These individuals would have the means to travel to specialists or see physicians that are not covered by their insurance. That would allow them to find the effective treatments sooner, which could help to lessen their symptoms. Additionally, a higher household income could allow for several resources and supports that would permit the patient to exert themselves less or pace better (i.e. stay within their energy envelope), which could result in experiencing PEM less than those individuals who do not have this financial support system. Such factors could include being able to work less outside of the home, afford access to higher quality health care, afford better quality food, and employ assistants to help with household tasks or

help with daily care for the patient. Deale and Wessely (2001) found that many patients are unsatisfied with the level of care they receive and often report disagreement on the diagnosis, receive a misdiagnosis, or experience dismissive or unknowledgeable doctors. Patients with higher income may be able to travel further or pay to see out-of-network physicians that specialize in ME and CFS care, which could help reduce the severity of their symptoms since the physician is knowledgeable about possible treatments or pacing. Alternatively, it is possible that individuals with lower factor scores, less frequent and severe symptoms, are physically well enough to hold employment, thus leading to an increase in household income.

The differences found between married or living with a partner and the individuals that are separated, divorced, or widowed may suggest a lack of family support has negative consequences for the course of ME and CFS. Schweitzer et al. (1995) found that 43% of CFS patients reported that their family initially did not accept their diagnosis as being a valid illness, which caused a strain on their relationships. However, once the family accepted the illness as being legitimate, they would help provide care and support when symptoms become more severe and affected functioning. Additionally, it is possible that some of the patients that are not married or living with a partner may not have had the energy available to maintain relationships or have been abandoned by partners due to their illness severity. Patients that do not have this social support built into their everyday lives due to divorce, separation, or death of a spouse may not have the means to take care of themselves during periods of increased illness severity. As a result, they may have to continue over-exerting themselves, thus exacerbating their symptoms even further.

This study has several limitations. Participants represent a convenience sample of individuals who self-reported an ME or CFS diagnosis. As such, there was no certain case definition which the patients were required to meet to be included in the study. The sample was also predominantly Caucasian. Community samples differ from this study's sample in that they include more ethnic minorities and individuals of lower socioeconomic status, which may have an effect on their symptomatology (Jason et al., 1995). Finally, the study included individuals from multiple countries. Zdunek et al. (2015) found differences in functioning level and symptom severity between samples collected in the United States and samples collected in the United Kingdom. It was suggested that differences in healthcare systems and resource availability could lead to contrasting findings from research conducted in different geographic locations. A multinational, cross-cultural study would create a heterogeneous sample that would make it difficult to parse out cultural differences that affect the symptomatology of ME and CFS. However, the heterogeneity of our sample may be an advantage as it could allow us to generalize the current findings across several settings and geographic locations. Future research should attempt to confirm these findings using a more homogenous patient population with a standardized recruitment setting and diagnostic criteria.

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Table 1

Factor loadings for each post-exertional malaise item (N = 648)

	Factor	
	General	Muscle
Post-exertional malaise ¹	.832	
Prolonged generalized fatigue or malaise following previously tolerable levels of exercise ¹	.822	
Post-exertional exhaustion that is immediate or delayed ³	.820	
Symptoms worsen with exertion ³	.816	
Substantial reduction in pre-illness activity level due to low threshold physical and mental fatigability ³	.758	
Fatigue/extreme tiredness ²	.715	
Marked, rapid physical or cognitive fatigability in response to exertion ³	.688	
Exhaustion not relieved by rest ³	.666	
Prolonged worsening of symptoms after physical activity ⁴	.612	
Minimum exercise makes you physically tired ²	.609	
Physically drained or sick after mild activity ²	.576	
Mentally tired after the slightest effort ²	.529	
Muscle weakness after minor exertion ⁴		.926
Muscle fatigability after minor exertion ⁴		.906
Muscle pain after minor exertion ⁴		.810
Next day soreness or fatigue after non-strenuous, everyday activities ²		.420
Dead, heavy feeling after starting to exercise ²		.409

Question sources:

¹CDC (Reyes et al., 2003)²DSQ (Jason et al., 2010)³ME-ICC (Carruthers et al, 2011)⁴Ramsay (Ramsay, 1988)

Table 2

Correlation and mean factor scores by demographic and functional status

	General Factor	Muscle Factor
Pearson Correlations		
SF-36 Physical Functioning	−0.612 **	−0.610 **
Bell Ability Scale	−0.643 **	−0.560 **
Age	−0.064	0.000
Mean Factor Scores		
Gender		
Male	0.036	−0.174
Female	0.002	0.027
Race		
White/Caucasian	0.003	0.005
Minority	−0.046	−0.108
Ethnicity		
Hispanic	0.135	0.160
Non-Hispanic	0.002	−0.001
Residence		
United States	−0.043	−0.200
International	−0.052	−0.050
Marital Status		
	*	*
Married/Living with Partner	−0.099	−0.081
Separated, Divorced, Widowed	0.167	0.186
Never Married	0.102	0.058
Education Level		
	**	**
High School or Less	0.229	0.304
Partial College	0.153	0.230
College Degree	−0.094	−0.138
Graduate/Professional Degree	−0.090	−0.115
Current Work Status		
	**	**
On Disability	0.243	0.236
Student	−0.150	0.151
Homemaker	0.026	0.052
Retired	−0.012	−0.086
Unemployed	0.254	0.174
Working Part-Time	−0.660	−0.659
Working Full-Time	−0.518	−0.324
Household Income		
	**	**
Less than \$24,999	0.174	0.225
\$25,000 to \$49,999	−0.106	−0.107

	General Factor	Muscle Factor
\$50,000 to \$99,999	−0.037	−0.030
\$100,000 to \$149,999	−0.176	−0.329
\$150,000 or more	−0.382	−0.428

*
 $p < .05$,

**
 $p < .01$

Table 3

Percentage of patients meeting a 2–2 threshold for PEM symptoms

	All Patients
	(N = 704)
	% (N)
Any PEM Symptoms	99.6 (701)
General Factor	99.3 (699)
Fatigue/extreme tiredness	94.2 (663)
Symptoms worsen with exertion	91.6 (645)
Substantial reduction in pre-illness activity level due to low threshold physical and mental fatigability	90.9 (640)
Post-exertional exhaustion that is immediate or delayed	89.6 (631)
Post-exertional malaise	89.2 (628)
Prolonged generalized fatigue or malaise following previously tolerable levels of exercise	88.1 (620)
Minimum exercise makes you physically tired	86.6 (610)
Physically drained or sick after mild activity	85.7 (603)
Prolonged worsening of symptoms after physical activity	84.5 (595)
Exhaustion not relieved by rest	84.2 (593)
Marked, rapid physical or cognitive fatigability in response to exertion	83.5 (588)
Mentally tired after the slightest effort	80.3 (565)
Muscle Factor	94.9 (668)
Next day soreness or fatigue after non-strenuous, everyday activities	85.5 (602)
Muscle fatigability after minor exertion	82.0 (577)
Dead, heavy feeling after starting to exercise	81.0 (570)
Muscle weakness after minor exertion	75.9 (534)
Muscle pain after minor exertion	68.2 (480)