

## Two Symptoms Accurately Identify Post-exertional Malaise in Myalgic Encephalomyelitis/ Chronic Fatigue

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**Background:** The diverse manifestations of post-exertional malaise (PEM) may make it difficult to recognize. Development of brief, accurate instruments for detecting PEM is critical for progress clinically and scientifically.

**Objectives:** To develop a clinical prediction rule for PEM

**Method:** 49 ME/CFS (Fukuda- or physician-diagnosed) and 10 healthy, sedentary subjects each completed 2 maximal cardiopulmonary exercise tests separated by 24 hours. During 5 different times (immediately and 24 hours after each test, 7 days from study initiation), subjects reported symptoms via an open-ended questionnaire. Two reviewers blinded to diagnosis classified responses into 19 symptom categories. Next, using receiver operating characteristics curve analyses, we calculated the area under the curve (AUC) value of each symptom category to predict group membership at each and any time point. A similar method was applied to determine the number of symptoms yielding the highest sensitivity and specificity. Finally, symptom categories with significant AUC values were entered into a binary logistic regression model to determine which symptom categories best distinguished ME/CFS from control subjects. A two-tailed p-value  $\leq 0.05$  was deemed significant.

**Results:** For all time points, only 2-4 symptom categories were needed to accurately diagnose PEM. During different time points, fatigue, cognitive problems, and lack of positive feelings/ mood showed up consistently although in different combinations to predict membership in the ME/CFS group. For the overall time period, binary logistic regression revealed decrease in function and a lack of positive feelings/mood as being independently and significantly predictive of group membership ( $p < 0.001$ ). This 2-symptom model classified 89.8% of ME/CFS subjects and 72.7% of controls correctly with a  $r^2$  value of 53.7%.

**Conclusion:** Inquiring specifically about post-exertional decrease in function and lack of positive feelings/mood may help diagnose PEM quickly and accurately. Other features distinguishing PEM are cognitive dysfunction, fatigue, sleep disturbances, and persistence of symptoms beyond 24 hours. In the future, we hope to test and validate our findings in a larger sample of subjects.

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