Variability in prevalence and symptom response of post exertion malaise in Gulf War illness

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**Research Topic:** Pathobiology/Pathophysiology

**Introduction:** Post exertion malaise (PEM) is a commonly reported clinical feature of Gulf War illness (GWI) but has not been systematically studied under controlled laboratory settings. We have previously reported variable PEM responses in GWI 24-hrs post exercise, underscoring the need for research that more thoroughly characterizes the symptom response. The purpose of the present investigation was to examine symptom responses for one-week following acute aerobic exercise in Gulf War Veterans (GVs). Based on our prior work, we hypothesized that symptoms would be significantly exacerbated in GWI+ Veterans relative to healthy controls, but only in those reporting that PEM was part of their GWI symptom profile — identified during case definition screening.

**Methods:** Seventy-seven GVs [(n=44 GWI; Age: 52.1±4.2; BMI: 30.9±5.8) (n=33 GV Controls; Age: 52.3±5.2; BMI: 29.4±4.8)] completed a symptom inventory, based on the Kansas GWI Questionnaire, for one-week prior to and one-week following a 30-minute submaximal exercise challenge at 70% of heart rate reserve. GWI groups were stratified based on whether the Veteran endorsed experiencing PEM (n=26 GWI+; n=18 GWI-). Symptom responses were assessed using Linear Mixed Effects models with repeated measures for symptom measurement. Variability was preliminarily assessed via the interquartile range (IQR) statistic.

**Results:** There were significant Group-by-Time interactions for Fatigue (F=7.8, p=0.006), Muscle Pain (F=5.7, p=0.01), Unrefreshing Sleep (F=7.7, p=0.006), and Memory Problems (F=8.0, p=0.005), but not Gastrointestinal symptoms or Anxious Mood (p>0.05). GWI+ Veterans reported significantly (p<0.05) greater symptoms (e.g. fatigue severity, muscle pain, poor sleep) both prior to and following the exercise challenge than GWI- and Control groups. Moreover, GWI+ Veterans had a greater IQR for most of the symptoms that were assessed.

**Conclusions:** The symptom response to acute exercise is variable in terms the prevalence and type of symptom exacerbation. Research aimed at determining physiological predictors of PEM in GWI is needed to better understand the presence, nature, severity, and time-course of symptom responses. These studies will be critical for better understanding the pathophysiology of GWI, and towards establishing for whom exercise is safe and for whom it may be contraindicated.