



SHORT COMMUNICATION

# Stress management skills, cortisol awakening response, and post-exertional malaise in Chronic Fatigue Syndrome



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**Summary** Chronic Fatigue Syndrome (CFS) is characterized in part by debilitating fatigue typically exacerbated by cognitive and/or physical exertion, referred to as post-exertional malaise (PEM). In a variety of populations, the cortisol awakening response (CAR) has stood out as a marker of endocrine dysregulation relevant to the experience of fatigue, and may therefore be particularly relevant in CFS. This is the first study to examine PEM and the CAR in a sample of individuals with CFS. The CAR has also been established as a stress-sensitive measure of HPA axis functioning. It follows that better management of stress could modulate the CAR, and in turn PEM. In this cross-sectional study, we hypothesized that greater Perceived Stress Management Skills (PSMS) would relate to lower reports of PEM, via the impact of PSMS on the CAR. A total of 117 adults (72% female) with a CFS diagnosis completed self-report measures of PSMS and PEM symptomatology and a two-day protocol of saliva collection. Cortisol values from awakening and 30 min post-awakening were used to compute the CAR. Regression analyses revealed that greater PSMS related to greater CAR and greater CAR related to less PEM severity. Bootstrapped analyses revealed an indirect effect of PSMS on PEM via the CAR, such that greater PSMS related to less PEM, via a greater CAR. Future research should examine these trends longitudinally and whether interventions directed at improving stress management skills are accompanied by improved cortisol regulation and less PEM in individuals with CFS.

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Chronic Fatigue Syndrome (CFS) is a poorly understood medical condition, characterized in part by profound chronic fatigue as well as an acute increase in fatigue following exertion, referred to as post-exertional malaise (PEM). Given the paucity of effective treatments for CFS, there is an ongoing search for potential intervention targets based on the limited understanding of the mechanisms that govern symptom expression. One plausible target is neuroendocrine regulation, which can be reflected in patterns of cortisol secretion from the hypothalamic-pituitary-adrenal (HPA) axis. Patients with CFS are known to show a pattern of hypocortisolism, accompanied by an attenuated cortisol awakening response (CAR; Powell et al., 2013). Results of two recent meta-analyses found that, of measures of cortisol dysregulation, the CAR is most relevant to the experience of fatigue, including greater burnout and exhaustion, and may therefore be particularly relevant in CFS (Chida and Steptoe, 2009; Powell et al., 2013). To date, less attention has been paid to relationships between cortisol dysregulation and PEM. Whether an attenuated CAR relates to greater PEM in the context of CFS remains untested. This study fills that gap in the literature by examining the relationship between the CAR and PEM in patients presenting with CFS.

Importantly, PEM may be distally influenced by a variety of psychosocial factors such as stress and negative mood (Lutgendorf et al., 1995; Morris and Maes, 2013). Conversely, having greater Perceived Stress Management Skills (PSMS), may relate to less PEM since PSMS has been related to less fatigue in CFS patients in prior work (Lattie et al., 2012). Taken together, it is plausible that one's perceived ability to manage stress (PSMS) may influence symptoms such as PEM by modulating one's CAR, reflecting HPA-axis re-regulation. The present study thus examined the associations among PSMS, CAR, and PEM in persons diagnosed with CFS. We also examined the indirect relationship between PSMS and reports of PEM, via the CAR. It was hypothesized that higher PSMS would relate to lower reports of PEM, via the impact of PSMS on the CAR.

## 1. Methods

### 1.1. Participants and procedures

Participants in the present study were recruited for a larger study of stress and coping processes in persons with CFS. Preliminary findings from this study have been published elsewhere (Lattie et al., 2012). Participants were recruited via physician referral, support groups and special events including local CFS conferences, as well as via advertisements on CFS-related websites. In order to be eligible, participants were required to have a physician-determined CFS diagnosis according to the Centers for Disease Control and Prevention (CDC) criteria (Fukuda et al., 1994), to be fluent in English, live within the study area, have an active home telephone line, and be between the ages of 21 and 75 years.

Potential participants could be excluded for cognitive impairment or if they met criteria for schizophrenia, bipolar disorder, or substance abuse, or were actively suicidal. The Short Portable Mental Status Questionnaire (Pfeiffer, 1975) was used to determine marked cognitive impairment and

participants were excluded if they demonstrated diminished cognitive capabilities, as indicated by having made four or more errors on this measure. Potential psychiatric exclusions were assessed using a brief screening (First et al., 2002) adapted from the Structured Clinical Interview for the DSM-IV (American Psychological Association, 2000). Participants were also excluded for the presence of a medical condition (e.g., AIDS, lupus, rheumatoid arthritis) that would influence biological processes associated with CFS symptomatology, or if they endorsed taking medications that could modulate immune and neuroendocrine functioning.

Eligible participants signed an informed consent form and were scheduled for a home visit by a study staff member. During the home visit, the study staff member administered a battery of measures regarding psychosocial status and CFS symptoms and provided the participant with 8 Salivette® tubes. Participants provided saliva samples from two consecutive weekdays within one week of the home visit. For each of the collection days, participants were asked to take a sample upon awakening, 30 min after awakening, at 4 pm and at 9 pm. Participants were also asked to self-report the time of sampling on the label of each salivette. Participants were instructed to abstain from eating or drinking before and between the first two samples each day, and to avoid eating a large meal an hour before the afternoon and evening samples. Participants were also asked to avoid alcohol for at least 12 h prior to sample collection and to avoid vigorous exercise on sample collection days. Following the collection of samples, participants were instructed to freeze the Salivette® tubes in their home freezers in order to keep the salivary cortisol stable until it was retrieved by a member of the study staff. The present study only focused on the awakening and 30 min post-awakening saliva samples.

### 1.2. Measures

#### 1.2.1. Perceived Stress Management Skills (PSMS)

The Measure of Current Status (MOCS; Carver, 2006) was used to assess PSMS. Items on the MOCS are based on personal characteristics and behaviors that are associated with efficient stress management abilities, such as "I am able to use mental imagery to reduce any tension I experience" and "I can clearly express my needs to other people who are important to me." Participants were asked to rate their perceived ability to appropriately respond to challenges and demands of daily life on a 5 point scale which ranged from "1 – I cannot do this at all" to "5 – I can do this extremely well." The 17 items on the MOCS were summed to compose an overall stress management skill measure, with higher scores indicating greater PSMS (Penedo et al., 2006). In the present sample, the MOCS demonstrated a high degree of internal consistency (Cronbach's  $\alpha = .85$ ).

#### 1.2.2. Post-exertional malaise (PEM)

The PEM item from the CDC CFS Symptom Inventory (Wagner et al., 2005) was used to measure PEM symptoms over the past month. Participants were asked to rate on two separate five point scales the frequency ("1 – A Little of the Time" to "5 – All of the Time") and intensity ("1 – Very Mild" to "5 – Very Severe") of "Unusual fatigue following exertion that lasts for at least 24h. The frequency and intensity scores

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