

# Childhood Trauma and Risk for Chronic Fatigue Syndrome

## Association With Neuroendocrine Dysfunction

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**Context:** Childhood trauma appears to be a potent risk factor for chronic fatigue syndrome (CFS). Evidence from developmental neuroscience suggests that early experience programs the development of regulatory systems that are implicated in the pathophysiology of CFS, including the hypothalamic-pituitary-adrenal axis. However, the contribution of childhood trauma to neuroendocrine dysfunction in CFS remains obscure.

**Objectives:** To replicate findings on the relationship between childhood trauma and risk for CFS and to evaluate the association between childhood trauma and neuroendocrine dysfunction in CFS.

**Design, Setting, and Participants:** A case-control study of 113 persons with CFS and 124 well control subjects identified from a general population sample of 19 381 adult residents of Georgia.

**Main Outcome Measures:** Self-reported childhood trauma (sexual, physical, and emotional abuse; emotional and physical neglect), psychopathology (depression, anxiety, and posttraumatic stress disorder), and salivary cortisol response to awakening.

**Results:** Individuals with CFS reported significantly higher levels of childhood trauma and psychopathological symptoms than control subjects. Exposure to childhood trauma was associated with a 6-fold increased risk of CFS. Sexual abuse, emotional abuse, and emotional neglect were most effective in discriminating CFS cases from controls. There was a graded relationship between exposure level and CFS risk. The risk of CFS conveyed by childhood trauma further increased with the presence of posttraumatic stress disorder symptoms. Only individuals with CFS and with childhood trauma exposure, but not individuals with CFS without exposure, exhibited decreased salivary cortisol concentrations after awakening compared with control subjects.

**Conclusions:** Our results confirm childhood trauma as an important risk factor of CFS. In addition, neuroendocrine dysfunction, a hallmark feature of CFS, appears to be associated with childhood trauma. This possibly reflects a biological correlate of vulnerability due to early developmental insults. Our findings are critical to inform pathophysiological research and to devise targets for the prevention of CFS.

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**C**HRONIC FATIGUE SYNDROME (CFS) affects up to 2.5% of the US adult population,<sup>1-3</sup> with an estimated total economic loss of \$9.1 billion per year.<sup>4</sup> The causes and pathophysiology of CFS remain unknown and effective prevention is elusive. Identifying risk factors for CFS is critical to guide pathophysiological research and to devise targets for prevention. Risk factors of CFS identified in prior studies include female gender, genetic disposition, and certain personality traits or behavioral styles.<sup>5</sup> Moreover, physical and emotional stressors are risk or triggering factors of CFS.<sup>5</sup> Stress in interaction with other risk factors likely triggers CFS symptoms through its effects on central ner-

vous, neuroendocrine, and immune systems, resulting in functional changes that lead to fatigue and associated symptoms such as sleep disruption, cognitive impairment, and pain.<sup>6</sup> However, obviously not every individual exposed to a stressor goes on to develop CFS, and it is therefore of critical importance to understand sources of individual differences in vulnerability to the pathogenic effects of stress.

We previously suggested that early adverse experience such as childhood abuse, neglect, and loss might be a predisposing factor that interferes with successful adaptation to stress, thereby conveying risk to develop CFS.<sup>7</sup> This hypothesis was based on evidence from developmental neurosciences suggesting that stress early in life within a genetic window of vulnerability

