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Fatigue and Disrupted Sleep-Wake Patterns in Patients With Cancer: A Shared Mechanism

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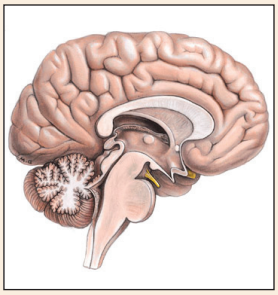

The strong and potentially reciprocal relationship between cancer-related fatigue (CRF) and disrupted sleep-wake patterns suggests a possible shared physiologic pathway. A growing body of evidence supports this and shows that abnormalities in the 24-hour rhythm of stress-related hormones may be related to chronic fatigue and sleep disturbances. Aberrations in the hypothalamic-pituitary-adrenal (HPA) axis, the primary neuroendocrine interface responding to stress, induce important biologic and behavioral consequences. HPA aberrations have long been associated with chronic fatigue syndrome. Many overlapping symptoms exist between chronic fatigue syndrome and CRF, including sleep disruption. Therefore, in the absence of knowledge about CRF mechanisms, emerging biologic models from chronic fatigue syndrome may assist in understanding the cause of CRF. Cancer-associated stressors also may alter the circadian functions of HPA-associated neuroendocrine activities, which result in the symptoms of fatigue and disrupted sleep-wake patterns in patients with cancer. Exploring promising physiologic models furthers the knowledge about CRF and disrupted sleep and may foster hypothesis-based studies of mechanisms that underlie apparent overlapping symptoms, providing the basis for new management to improve sleep and lessen fatigue.

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Cancer-related fatigue (CRF) is a significant clinical problem that occurs across the spectrum of cancer diagnoses, major cancer therapies, and the entire illness trajectory. CRF is highly prevalent not only among patients undergoing cancer treatment, but also cancer survivors (Alexander, Minton, Andrews, & Stone, 2009; Barbera et al., 2010; Byar, Berger, Bakken, & Cetak, 2006; Curt et al., 2000; Davidson, MacLean, Brundage, & Schulze, 2002; Flechtner & Bottomley, 2003; Fleming, Gillespie, & Espie, 2010; Johansson, Wilson, Brunton, Tishelman, & Molassiotis, 2010; Kirkova et al., 2010; Langeveld, Grootenhuis, Voute, de Haan, & van den Bos, 2003; Quick & Fonteyn, 2005; Reinertsen et al., 2010). Disrupted sleep patterns often are concurrent with fatigue in cancer; an estimated 31% of fatigued patients with cancer experience frequent insomnia (Sarna, 1993). Fatigue and disrupted sleep affect all aspects of life for patients with cancer (Alexander et al., 2009; Byar et al., 2006; Davidson et al., 2002; Fleming et al., 2010; Fortner, Stepanski, Wang, Kasprowicz, & Durrence, 2002; Grunfeld & Cooper, 2010; Redeker, Lev, & Ruggiero, 2000; Rosedale & Fu, 2010; Scott, Lasch, Barsevick, & Piault-Louis, 2011). Their coexistence heightens symptom distress (Sarna, 1993) and further decreases the patient's ability to function. As a consequence, quality of life suffers. Fatigue and disrupted sleep are severely impairing, and neither symptom has been controlled fully in patients with cancer, largely because of a lack of knowledge about the underlying mechanisms.

The growing recognition of symptom clusters (Cleeland et al., 2000; Dodd, Miaskowski, & Lee, 2004) has led to speculation of common biologic pathways underlying some of the symptoms related to cancer (Cleeland et al., 2003; Lee et al., 2004). In addition to the frequent co-occurrence of fatigue and disrupted sleep, the two symptoms demonstrate a strong and possibly reciprocal relationship (Pud et al., 2008; Roscoe et al., 2007). Patients with CRF are more susceptible to sleep problems than their nonfatigued counterparts (Alexander et al., 2009; Davidson et al., 2002; Okuyama et al., 2001), and higher CRF levels are associated with more sleep disturbances (Alexander et al., 2009; Andrykowski, Curran, & Lightner, 1998; Berger, 1998; Berger & Farr, 1999; Berger & Higginbotham, 2000; Cheng & Lee, 2011; Davidson et al., 2002; Okuyama et al., 2001; Redeker et al., 2000).