Factors Associated With Sleep-Wake Disturbances in Child and Adult Survivors of Pediatric Brain Tumors: A Review

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Pediatric brain tumors are the most common solid tumors in pediatric patients (younger than aged 19), with an annual incidence rate of about 3 cases per 100,000 in the United States (Gurney, Smith, & Bunin, 1999). Because of technological advances in radiation therapy and aggressive chemotherapy regimens, the five-year relative survival rates are approaching 75% (Jemal et al., 2006). Invasive surgery and high-dose radiation therapy remain essential components of a long-term cure (Packer, 1999; Packer, Cogen, Vezina, & Rorke, 1999). After these intense cancer treatments, about 50% of brain tumor survivors, in some samples, experienced sleep-wake disturbances as long-term sequelae (Muller, Handewerker, Wollny, Faldum, & Sorensen, 2002; Palm et al., 1992; Van Someren et al., 2004). In follow-up studies of brain tumor survivors, sleep impairment negatively affected quality of life (Anderson et al., 2001; Hudson et al., 2003; Mostow, Byrne, Connelly, & Mulfihill, 1991; Pelletier, Verhoef, Khatri, & Hagen, 2002). To date, little research in adult survivors (aged older than 18 years) of pediatric brain tumors is available to guide sleep interventions and improve daytime functioning. The purpose of this review is the identification of critical factors associated with sleep-wake disturbances in child and adult survivors of pediatric brain tumors.

**Background**

A key contributor affecting sleep-wake disturbances in brain tumor survivors is destruction of the hypothalamus, a radio-sensitive sleep-wake structure susceptible to long-term damage (Constine et al., 1993; Heikens et al., 1998). Cranial radiation therapy alters the hypothalamic-pituitary axis, with associated hormonal abnormalities and neurocognitive, sensory, and motor defects, as well as impaired sleep patterns (Constine et al.). Radiation dose and age at treatment affect the severity of sequelae (Anderson et al., 2001; Fagioli, Brauner, & Rappaport, 1991; Packer et al., 1999).

Reported sleep disturbances in brain tumor survivors include insomnia, excessive daytime sleepiness, limb movement disorders, sleep apnea, and increased nighttime awakenings (di Gennaro et al., 2004; Marcus, Trescher, Halbower, & Lutz, 2002; Szucs, Bodizs, Barsi, & Halasz, 2001; Zembelis, Paparrigopoulos, & Saldatos, 2002). Impairment of hypocretin-producing cells in the lateral and posterior hypothalamus increases somnolence and promotes secondary narcolepsy in some survivors (Arii et al., 2001; Nishino, Ripley, Overeem, Lammer, & Mignot, 2000; Selbach & Haas, 2006; Taheri,