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

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Purpose/Objectives: To identify factors associated with sleep-wake disturbances in pediatric and adult survivors (aged older than 18 years) of pediatric brain tumors.

Data Sources: A computerized literature search was completed using MEDLINE®, CINAHL®, CancerLit, Dissertation Abstracts International, and PsycINFO. The search and a personal communication with one author discovered 25 English-language research articles and case reports describing sleep-wake patterns in brain tumor survivors from 1966–2008.

Data Synthesis: Disease- and treatment-related factors from direct injury to the hypothalamus results in irregular melatonin secretion and low hypocretin levels. This contributes to decreased daytime alertness, which remains the most reported sleep-wake disturbance in brain tumor survivors. Patients with craniopharyngiomas, radiation dose more than 3,500 cGy, and younger age at time of treatment experienced more severe sleep dysfunction.

Conclusions: Patients with brain tumors experience a disruption of sleep-wake patterns associated with major dysfunction in the hypothalamic-pituitary axis, affecting both Process S (homeostasis) and Process C (circadian) from the Two-Process Model of Sleep Regulation. Various demographic-, disease-, and treatment-related variables are involved in driving the onset of sleep disturbances. Interventions are needed to improve daytime function and decrease the effect of sleep disturbances on quality of life.

Implications for Nursing: Current sleep literature has identified patterns of sleep disturbances in cross-sectional studies of brain tumor survivors. Rigorous longitudinal designs are needed for future studies to detect onset patterns and trajectory of sleep-wake disorders. Intervention studies are needed to impact excessive daytime sleepiness, irregular sleeping and waking patterns, and other identified sleep-wake disorders.

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, & Sorenson, 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, & Mulvihill, 1991; Pelletier, Verhoef, Khatri, & Hagen, 2002). To date, little research in adult survivors (aged 19 years and older) 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, & Soldatos, 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,