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Food craving and obesity in survivors of pediatric ALL and lymphoma

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ABSTRACT

Cancer treatment can impact the hypothalamic-pituitary region of the developing brain, impairing appetite regulation and causing food craving in children who have survived cancer. We assessed food craving using a modified Food Craving Inventory in 22 survivors of pediatric acute lymphoblastic leukemia (ALL) and lymphoma (median age = 11.7 years) and evaluated its association with treatment exposure and changes in weight status over a one-year period. Mean total craving score was 2.1 (SD = 0.7). Survivors reported significantly higher mean craving score for fast-foods [2.6 (SD = 0.9)] than for sweets [2.1 (SD = 0.8)], carbohydrates [2.0 (SD = 0.6)], and fats [1.8 (SD = 0.7)] (all P values < 0.05). Results from multivariate linear regression indicated that survivors diagnosed at an older age (≥4.5 years) experienced higher frequencies of food craving than those diagnosed at a younger age (<4.5 years) (β = 0.88, 95% CI: 0.42, 1.34). Food craving, however, was not significantly associated with survivors' weight status over 12 months of follow-up. Food craving alone does not appear to explain the obesity risk in this sample of childhood cancer survivors. The role of food craving in shaping eating behavior and obesity risk needs to be further evaluated in a large cohort of childhood cancer survivors.

1. Introduction

Dramatic improvements in the diagnosis and treatment of cancer in childhood have led to a rapidly growing cohort of survivors, now estimated to exceed 420,000 (Mariotto et al., 2009; Robison & Hudson, 2014). However, following successful treatment for cancer, a large proportion of childhood cancer survivors become overweight or obese (Garmey et al., 2008; Green et al., 2012; Zhang et al., 2014; Zhang, Liu, Chung, & Kelly, 2015). Obesity adds additional risks to the chronic health conditions already experienced by childhood cancer survivors (Butturini et al., 2007; Hudson et al., 2013; Oeffinger et al., 2006). The causative factors leading to this increased obesity risk are not entirely understood.

There are several hypotheses regarding the mechanisms by which childhood cancer survivors have an increased susceptibility to weight gain (Jansen, Postma, Stolk, & Kamps, 2009; Kohler, Moon, Wright, Willows, & Davies, 2011; Mayer, Reuter, Dopfer, & Ranke, 2000; Reilly et al., 2001; Sklar et al., 2000; Skoczen et al., 2011). Central nervous system-directed therapy (e.g., cranial irradiation therapy and/or intrathecal chemotherapy) can directly damage the hypothalamic-pituitary region, impairing signaling reception from hormones that regulate hunger, appetite, and body fat homeostasis, such as ghrelin and leptin (Oeffinger et al., 2003; Samaan, Thabane, Burrow, Dillenburg, & Scheinemann, 2013; Sklar et al., 2000; von Deneen & Liu, 2011). These hormonal changes may affect food intake and appetite control via food craving (Chao, Grilo, White, & Sinha, 2014; Harvey, Wing, & Mullen, 1993; Lafay et al., 2001; Lustig et al., 2003; von Deneen & Liu, 2011; Weingarten & Elston, 1990; White, Whisenhunt, Williamson, Greenway, & Netemeyer, 2002; Yu et al., 2013). However, the degree to which childhood cancer survivors experience food craving and the role of food craving in unhealthy weight gain has not been

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previously described in young survivors who are at high risk of obesity (Zhang, Rodday, et al., 2014).

The aim of this study was to evaluate food craving in young survivors of pediatric acute lymphoblastic leukemia (ALL) and lymphoma, the first and third most common cancers diagnosed in children and adolescents, respectively. We further evaluated whether patient and treatment characteristics were related to food craving, and whether food craving was associated with changes in weight status in this sample of childhood cancer survivors.

2. Methods

2.1. Participants

Eligible patients were identified from the records of the Pediatric Hematology/Oncology Clinic at the Floating Hospital for Children at Tufts Medical Center, Boston MA (Zhang, Roberts, et al., 2014; Zhang, Saltzman, et al., 2015). To be eligible, patients had to (1) be diagnosed with ALL or lymphoma before 21 years of age, (2) be between the ages of 3–25 years at study enrollment, and (3) had either completed all cancer treatment within the past 15 years and be in remission, or on-treatment and receiving maintenance therapy. Patients were excluded if they had relapsed, had undergone allogeneic bone marrow transplant, had conditions known to influence food intake or energy expenditure, or were pregnant or lactating.

For all participants, parents completed a self-administered questionnaire that asked for demographic information such as the child's age, sex, race/ethnicity, preferred spoken language in the household, parents' age, sex, education, marital status, household income, insurance status, and their relationship with the child. Medical records were reviewed for each participant to extract cancer-related information including cancer diagnosis, medical history, and treatment information using the Summary of Cancer Treatment Form, developed by the Children's Oncology Group (Children's Oncology Group, 2013). Levels of total energy expenditure were measured using the doubly labeled water method at baseline, as described elsewhere (Zhang, Roberts, et al., 2014). Dietary intake was assessed by a set of three 24-h diet recalls (two weekdays and one weekend day) and a Block Food Frequency Questionnaire at baseline, 6 months and 12 months follow-up visits (Zhang, Saltzman, et al., 2015).

2.2. Procedure

We assessed food craving in childhood cancer survivors using a modified Food Craving Inventory (FCI) at baseline, 6 months and 12 months. The FCI assesses the subjective experience of craving across 28 different foods during the past month (White et al., 2002). Craving is defined as an intense desire to consume a particular food (or food type) that is difficult to resist. The frequency of craving is measured using 5- point Likert scale: 1 = never, 2 = rarely, 3 = sometimes, 4 = often, and 5 = always/almost every day. Because previous research has documented considerable errors in recalls of dietary intake by children 12 years old or under, (Livingstone, Robson, & Wallace, 2004) for participants ≤12 years, the FCI was modified to ask parents to report whether they observed or were told by their child that he/she experienced craving for a particular food or food type that is difficult to resist in the past month. The craving score for individual foods was averaged to calculate the mean total score and mean score for each of the four subscales/components: (1) high fats (including 8 foods), (2) sweets (including 8 foods), (3) carbohydrates/starches (including 8 foods), and (4) fast-food fats (including 4 foods) (the last two will be abbreviated as carbohydrates and fast-foods, respectively, for the remainder of this article) (Supplemental Table 1). For total craving and craving for each subscale/component, the minimum score is 1 and the maximum score is 5, with higher scores corresponding to higher frequency of craving (Martin, O'Neil, Tollefson, Greenway, & White, 2008; White et al., 2002). Previous studies have demonstrated that the FCI has reasonable test-retest reliability and validity to measure food craving (Martin et al., 2008; White & Grilo, 2005; White et al., 2002).

Weight and height were measured at baseline, 6 months and 12 months. Non-fasting weight was measured in light clothing, without shoes, on a standing scale to the nearest 0.1 kg. Height was measured using a wall-mounted stadiometer in conjunction with a headboard to the nearest 0.1 cm.

2.3. Statistical analysis

We first performed descriptive analyses for food craving at three time points (baseline, 6 months, and 12 months) and examined longitudinal trends in food craving over the one-year follow-up period. Because no significant trend was identified over time, we averaged craving scores at the three time points to improve reliability. Next, we examined food craving scores in association with patient and treatment characteristics using Analysis of Variance (ANOVA) and multivariate linear regression. Because interval since therapy was highly correlated with age at enrollment, i.e., survivors with a longer interval since therapy were also those who were older at study enrollment, given the limited sample size, we chose not to include both variables in the same regression model (i.e. only age at enrollment was analyzed in the multivariate linear regression model along with other patient and treatment characteristics). The cumulative dose of steroids was calculated by converting the dexamethasone dose to a prednisone equivalent dose (1 mg dexamethasone = 6.67 mg prednisone) and summing across the two medications (Baker et al., 2013). For patients aged 3–20 years old, BMI z-score was calculated based on age- and sex-specific BMI cut-offs in the 2000 Center for Disease Control and Prevention (CDC) growth charts (Centers for Disease Control and Prevention, 2000). For patients >20 years, BMI z-score and percentile were calculated based on the reference data for age 20 in the 2000 CDC growth charts (Esbenshade et al., 2011). The BMI z-score indicates the number of standard deviations the measurement is away from the mean for the age- and sex-specific US general population mean. A BMI z-score >0 indicates a higher-than-median BMI. Obesity was defined as BMI z-score ≥1.645 (≥95th percentile), overweight as BMI z-score = 1.036–1.644 (85th–94.9th percentile), and healthy weight as BMI z-score = −1.645 to 1.035 (5th–84.9th percentile), based on the current recommendations of the US CDC (Barlow, 2007) and in accordance with previous studies (Hedley et al., 2004). Last, we performed repeated measure models to evaluate whether food craving independently predicted weight patterns over 12 months after controlling for patient and treatment characteristics (Lindsey, 1999). All statistical tests were two-sided with a significance level of 0.05. All analyses were performed using SAS (version 9.3; SAS Institute Inc., Cary, NC, USA).

The study was approved by the institutional review board at Tufts Medical Center/Tufts University. For patients under 18 years of age, parent consent and child assent were obtained prior to enrollment. Patients who had reached the age of majority (18 years) provided consent for their own participation.

3. Results

Of the 67 eligible patients, 22 agreed to participate in the study, including 17 diagnosed with pediatric ALL and 5 diagnosed with lymphoma (Table 1). The median age at diagnosis was 4.9 (range: