Published in final edited form as:

Appetite. 2016 January 1; 96: 1–6. doi:10.1016/j.appet.2015.08.039.

Food Craving and Obesity in Survivors of Pediatric ALL and Lymphoma

Marissa Shams-White, MS, MPH^a, Michael J. Kelly, MD, MPH, MS^{b,c}, Cheryl Gilhooly, PhD, MPH, RD^d, Shanshan Liu, MS, MPH^a, Aviva Must, PhD^e, Susan K. Parsons, MD, MRP^{b,f,g}, Edward Saltzman, MD^{a,d}, and Fang Fang Zhang, MD, PhD^{a,d}

^aDepartment of Nutrition Sciences, Friedman School of Nutrition Science and Policy, Tufts University, Boston, MA, USA

^bDepartment of Pediatrics, Tufts University School of Medicine, Boston, MA

^cDivision of Pediatric Hematology/Oncology, The Floating Hospital for Children, Tufts Medical Center, Boston, MA, USA

^dJean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, Boston, MA, USA

^eDepartment of Public Health and Community Medicine, Tufts University School of Medicine, Boston, MA, USA

^fDepartment of Medicine, Tufts University School of Medicine, Boston, MA

^gInstitute for Clinical Research and Health Policy Studies, Tufts Medical Center, Boston, MA

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) ($\beta=0.88$, 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

Corresponding author: Fang Fang Zhang, MD, PhD, Department of Nutrition Science, Friedman School of Nutrition Science and Policy, Tufts University, 150 Harrison Ave, Boston, MA 20111 (fang_fang.zhang@tufts.edu). Phone: 617-636-3704; Fax: 617-636-3727.

Disclosure: The authors have no conflict of interests to disclose.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

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.

Keywords

Food craving; obesity; childhood cancer; nutrition

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; F.F. 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, & Scheinmann, 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 previously described in young survivors who are at high risk of obesity. (F. F. Zhang, A. M. 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.

METHODS

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. (F. F.

Zhang, S. B. 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. (F. F. Zhang, S. B. Roberts, et al., 2014) Dietary intake was assessed by a set of three 24-hour 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)

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 MB, Oct 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 scores 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.

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 – 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.

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: 3.1–7.0) years, the median age at study enrollment was 11.7 (range: 4.7–24.9) years, and the median interval from diagnosis was 5.6 (range: 0.3–17.0) years. The majority

of the participants were male (68%) and non-Hispanic-white (77%). About 40% were overweight or obese at study enrollment.

No significant change in food craving was observed from baseline to 6 months and 12 months follow-up (Figure 1). When food craving reported at three time points were averaged, the mean total craving score in the 22 survivors was 2.1 (SD=0.7), and the mean score for each subscale, from the highest to the lowest, was 2.6 (SD=0.9) for fast-foods, 2.1 (SD=0.8) for sweets, 2.0 (SD=0.6) for carbohydrates, and 1.8 (SD=0.7) for fats. Participants reported significantly more frequent cravings for fast-foods than cravings for sweets ($P=0.003$), carbohydrates ($P=0.0007$), and fats ($P<0.0001$). Individual foods that survivors craved most frequently were chips (mean=2.7; SD=1.1), pizza (mean=2.6; SD=1.2), French fries (mean=2.5; SD=1.1), pasta (mean=2.5; SD=1.0), and ice cream (mean=2.5; SD=1.4).

Compared to participants diagnosed at a younger age (< 4.5 years), those diagnosed at an older age (≥ 4.5 years) craved more frequently overall ($\beta = 0.88$, 95% CI: 0.42, 1.34) and for each of the subscales: fast-foods ($\beta = 0.97$, 95% CI: 0.29, 1.65), sweets ($\beta = 0.96$, 95% CI: 0.26, 1.66), carbohydrates ($\beta = 0.73$, 95% CI: 0.25, 1.20), and fats ($\beta = 0.87$, 95% CI: 0.31, 1.43) (Table 2). Participants treated with cranial irradiation therapy (CRT) had lower total craving ($\beta = -1.07$, 95% CI: -1.79, -0.34) and craving for fast-foods ($\beta = -1.65$, 95% CI: -2.73, -0.57), sweets ($\beta = -1.31$, 95% CI: -2.42, -0.20), and carbohydrates ($\beta = -0.88$, 95% CI: -1.63, -0.13) than those who did not received CRT. Age at enrollment, sex, weight status at enrollment, treatment status, interval since therapy, and cumulative steroid dose (i.e. cumulative dose of prednisone equivalents) was not significantly associated with food craving.

Sixteen participants (73%) completed the 6-month and 12-month follow-up visits, with no significant change in BMI z-score detected over 12 months ($\beta = -0.09$, $p=0.14$). After controlling for age at diagnosis and receipt of CRT, food craving including total craving and craving on each subscale were all associated with an increasing trend in BMI z-score over 12 months. However, none of the associations was statistically significant (Table 3). Survivors who were overweight or obese at 12 months ($n=6$) had similar mean craving scores compared to those who had healthy weight ($n=10$) [total craving: 2.09 (SD=0.36) vs. 2.11 (SD=0.68), $p=0.96$].

DISCUSSION

Childhood cancer survivors experience a high risk of obesity following cancer diagnosis and treatment. Cancer treatment received at a young age may directly impact survivors' eating behavior by causing craving for high energy-density foods. Our study is the first study to evaluate food craving and its association with weight status in a sample of childhood cancer survivors. We found survivors of pediatric ALL and lymphoma had cravings most frequently for fast-foods; however, food craving was not significantly associated with changes in weight status over 12 months.

Anecdotal observations from clinicians indicate that children crave high energy-density foods or salty foods while receiving cancer treatment. In our cohort of 22 survivors of

pediatric ALL and lymphoma who were approximately 5.6 years post-diagnosis, the highest craving score was also found for fast-foods, for which high energy density and salt content are often observed. The total craving score in survivors is comparable to that reported in 646 adults (mean age=30 years) in a community sample who were assessed for total food craving using the same FCI (mean=2.0; SD=0.7) (Chao et al., 2014). Patterns of food craving were also similar between our sample and the community sample (Chao et al., 2014), with fast-foods having the highest craving score, followed by sweets, carbohydrates, and fats. Frequent craving for fast-foods may lead to unhealthy eating patterns (e.g. a high consumption of calories and dietary sodium), which are well established risk factors for chronic health conditions. Indeed, craving for fast-foods was significantly correlated with fast-food consumption reported from food frequency questionnaires in this sample of childhood cancer survivors (Pearson correlation coefficient = 0.60, $p=0.04$).

When patient and treatment characteristics were examined, we found survivors diagnosed at 4.5 years or older experienced stronger craving than those diagnosed less than 4.5 yrs. A potential explanation could be that younger children were less likely to form food associations than older children when they were first diagnosed. Receipt of CRT may change taste preference and appetite by damaging the hypothalamic axis and taste receptors. (Cohen et al., 2014; Skolin et al., 2006) This can potentially result in a decrease in food craving in survivors treated with CRT. However, in our sample of childhood cancer survivors, only two participants received CRT. The small number of survivors treated with CRT limited our ability to formally assess whether survivors treated with CRT experience different frequencies and patterns of food craving compared to those treated without CRT. The observed difference needs to be interpreted with caution. Survivors who received a higher cumulative dose of steroids (4,000 mg/m²) tended to experience stronger craving than those treated with a lower dose (<4,000 mg/m²). However, the difference did not reach statistical significance. We also evaluated whether the use of different types of steroids (i.e., prednisone and dexamethasone) was associated with food craving and did not find significant associations. Future studies with a larger sample size are required to further investigate receipt of CRT, type and dose of steroids, and other treatment exposures as potential mechanisms for food craving in childhood cancer survivors.

Two previous studies (Burton, Smit, & Lightowler, 2007; Martin et al., 2008) that assessed food craving in overweight/obese individuals (mean BMI=35–38 kg/m²) using the same FCI found a higher total craving score (2.6) than that identified in individuals with a healthy weight, suggesting food craving may be positively correlated with BMI. Several cross-sectional studies (Chao et al., 2014) have observed positive associations between food craving and BMI but could not distinguish between food craving as a cause for obesity and food craving as a consequence of restrained eating in obese individuals. In our longitudinal investigation, total food craving and craving for each subscale were all related to an increasing trend in weight status over time, although none of the associations reached statistical significance. The null findings may be due to the lack of sufficient statistical power to detect such an association in this pilot study.

Several limitations of our study are noteworthy. First, the small sample size of this study may have insufficient statistical power to identify patient and treatment characteristics that

are associated with food craving. Second, the short length of follow-up (i.e., 12 months) may also prevent us from identifying a statistically significant impact of food craving on obesity risk in childhood cancer survivors. Third, our study lacked age- and sex-matched healthy controls, which does not allow us to formally assess the difference in food craving between childhood cancer survivors and the general population. Fourth, food craving was assessed based on a five-point Likert scale. The limited options of choice do not capture levels of food craving on a vast, multi-dimensional continuum. Last, our study included only survivors of childhood ALL or lymphoma and our findings may not be applicable to all survivors of childhood cancer. Despite these limitations, our study provides the first evidence suggesting frequent fast-foods craving in childhood cancer survivors, which if replicated would have important implications for obesity prevention in this high-risk population.

In summary, we report that childhood cancer survivors crave fast-foods more frequently than other food items. However, food craving was not significantly associated with weight status over 12 months in this sample of childhood cancer survivors. Future studies are needed to further evaluate the role of food craving in shaping eating behavior and obesity risk, as well as how treatment exposure affects food craving in the growing cohort of childhood cancer survivors.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Sources of support: All phases of this study were supported by the Boston Nutrition Obesity Research Center Grant Number P30DK46200, the National Center for Research Resources Grant Number UL1 RR025752, the National Center for Advancing Translational Sciences and the National Institutes of Health Grant Number UL1 TR000073. The funding source had no role in the design, conduct, or analysis of this study or the decision to submit the manuscript for publication.

We thank all participants of the Healthy Living Study, and Xi Lin, Geetika Dhaundiyal, Cathy McPherson, and Justin Wheeler for their assistances in coordinating study procedures.

References

- Baker KS, Chow EJ, Goodman PJ, Leisenring WM, Dietz AC, Perkins JL, Steinberger J. Impact of treatment exposures on cardiovascular risk and insulin resistance in childhood cancer survivors. *Cancer Epidemiol Biomarkers Prev.* 2013; 22(11):1954–1963.10.1158/1055-9965.epi-13-0610 [PubMed: 24008489]
- Barlow SE. Expert committee recommendations regarding the prevention, assessment, and treatment of child and adolescent overweight and obesity: summary report. *Pediatrics.* 2007; 120(Suppl 4):S164–192.10.1542/peds.2007-2329C [PubMed: 18055651]
- Burton P, Smit HJ, Lightowler HJ. The influence of restrained and external eating patterns on overeating. *Appetite.* 2007; 49(1):191–197.10.1016/j.appet.2007.01.007 [PubMed: 17349717]
- Butturini AM, Dorey FJ, Lange BJ, Henry DW, Gaynon PS, Fu C, Carroll WL. Obesity and outcome in pediatric acute lymphoblastic leukemia. *J Clin Oncol.* 2007; 25(15):2063–2069.10.1200/jco.2006.07.7792 [PubMed: 17513811]
- Centers for Disease Control and Prevention. CDC growth charts. 2000.

- Chao A, Grilo CM, White MA, Sinha R. Food cravings, food intake, and weight status in a community-based sample. *Eat Behav.* 2014; 15(3):478–482.10.1016/j.eatbeh.2014.06.003 [PubMed: 25064302]
- Children's Oncology Group. Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers. 2013. Retrieved October 1, 2014, from <http://www.survivorshipguidelines.org/>
- Cohen J, Laing DG, Wilkes FJ, Chan A, Gabriel M, Cohn RJ. Taste and smell dysfunction in childhood cancer survivors. *Appetite.* 2014; 75:135–140.10.1016/j.appet.2014.01.001 [PubMed: 24412664]
- Esbenshade AJ, Simmons JH, Koyama T, Koehler E, Whitlock JA, Friedman DL. Body mass index and blood pressure changes over the course of treatment of pediatric acute lymphoblastic leukemia. *Pediatr Blood Cancer.* 2011; 56(3):372–378.10.1002/pbc.22782 [PubMed: 20860019]
- Garmey EG, Liu Q, Sklar CA, Meacham LR, Mertens AC, Stovall MA, Oeffinger KC. Longitudinal changes in obesity and body mass index among adult survivors of childhood acute lymphoblastic leukemia: a report from the Childhood Cancer Survivor Study. *J Clin Oncol.* 2008; 26(28):4639–4645.10.1200/jco.2008.16.3527 [PubMed: 18824710]
- Green DM, Cox CL, Zhu L, Krull KR, Srivastava DK, Stovall M, Robison LL. Risk factors for obesity in adult survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. *J Clin Oncol.* 2012; 30(3):246–255.10.1200/jco.2010.34.4267 [PubMed: 22184380]
- Harvey J, Wing RR, Mullen M. Effects on food cravings of a very low calorie diet or a balanced, low calorie diet. *Appetite.* 1993; 21(2):105–115. [PubMed: 8285649]
- Hedley AA, Ogden CL, Johnson CL, Carroll MD, Curtin LR, Flegal KM. Prevalence of overweight and obesity among US children, adolescents, and adults, 1999–2002. *JAMA.* 2004; 291(23):2847–2850.10.1001/jama.291.23.2847 [PubMed: 15199035]
- Hudson MM, Ness KK, Gurney JG, Mulrooney DA, Chemitilly W, Krull KR, Robison LL. Clinical ascertainment of health outcomes among adults treated for childhood cancer. *JAMA.* 2013; 309(22):2371–2381.10.1001/jama.2013.6296 [PubMed: 23757085]
- Jansen H, Postma A, Stolk RP, Kamps WA. Acute lymphoblastic leukemia and obesity: increased energy intake or decreased physical activity? *Support Care Cancer.* 2009; 17(1):103–106.10.1007/s00520-008-0531-0 [PubMed: 18989711]
- Kohler JA, Moon RJ, Wright S, Willows E, Davies JH. Increased adiposity and altered adipocyte function in female survivors of childhood acute lymphoblastic leukaemia treated without cranial radiation. *Horm Res Paediatr.* 2011; 75(6):433–440.10.1159/000324412 [PubMed: 21464554]
- Lafay L, Thomas F, Mennen L, Charles MA, Eschwege E, Borys JM, Basdevant A. Gender differences in the relation between food cravings and mood in an adult community: Results from the fleurbaix laventie ville sante study. *Int J Eat Disord.* 2001; 29(2):195–204. [PubMed: 11429982]
- Lindsey, JK. *Models for Repeated Measurements.* 2. New York: Oxford University Press; 1999.
- Livingstone RP MB, Wallace JM. Issues in dietary intake assessment of children and adolescents. *Br J Nutr.* Oct; 2004 92(Suppl 2):S213–222. [PubMed: 15522159]
- Lustig RH, Post SR, Srivannaboon K, Rose SR, Danish RK, Burghen GA, Merchant TE. Risk factors for the development of obesity in children surviving brain tumors. *J Clin Endocrinol Metab.* 2003; 88(2):611–616.10.1210/jc.2002-021180 [PubMed: 12574189]
- Mariotto AB, Rowland JH, Yabroff KR, Scoppa S, Hachey M, Ries L, Feuer EJ. Long-term survivors of childhood cancers in the United States. *Cancer Epidemiol Biomarkers Prev.* 2009; 18(4):1033–1040.10.1158/1055-9965.epi-08-0988 [PubMed: 19336557]
- Martin CK, O'Neil PM, Tollefson G, Greenway FL, White MA. The association between food cravings and consumption of specific foods in a laboratory taste test. *Appetite.* 2008; 51(2):324–326.10.1016/j.appet.2008.03.002 [PubMed: 18417253]
- Mayer EI, Reuter M, Dopfer RE, Ranke MB. Energy expenditure, energy intake and prevalence of obesity after therapy for acute lymphoblastic leukemia during childhood. *Horm Res.* 2000; 53(4):193–199. [PubMed: 11044803]

- Oeffinger KC, Mertens AC, Sklar CA, Kawashima T, Hudson MM, Meadows AT. Childhood Cancer Survivor S. Chronic health conditions in adult survivors of childhood cancer. *N Engl J Med*. 2006; 355(15):1572–1582.10.1056/NEJMsa060185 [PubMed: 17035650]
- Oeffinger KC, Mertens AC, Sklar CA, Yasui Y, Fears T, Stovall M, Robison LL. Obesity in adult survivors of childhood acute lymphoblastic leukemia: a report from the Childhood Cancer Survivor Study. *J Clin Oncol*. 2003; 21(7):1359–1365. [PubMed: 12663727]
- Reilly JJ, Brougham M, Montgomery C, Richardson F, Kelly A, Gibson BE. Effect of glucocorticoid therapy on energy intake in children treated for acute lymphoblastic leukemia. *J Clin Endocrinol Metab*. 2001; 86(8):3742–3745. [PubMed: 11502805]
- Robison LL, Hudson MM. Survivors of childhood and adolescent cancer: lifelong risks and responsibilities. *Nat Rev Cancer*. 2014; 14(1):61–70.10.1038/nrc3634 [PubMed: 24304873]
- Samaan MC, Thabane L, Burrow S, Dillenburg RF, Scheinmann K. Canadian Study of Determinants of Endometabolic Health in CHILDrEn (CanDECIDE study): a cohort study protocol examining the mechanisms of obesity in survivors of childhood brain tumours. *BMJ Open*. 2013; 3(6)10.1136/bmjopen-2013-002869
- Sklar CA, Mertens AC, Walter A, Mitchell D, Nesbit ME, O’Leary M, Robison LL. Changes in body mass index and prevalence of overweight in survivors of childhood acute lymphoblastic leukemia: role of cranial irradiation. *Med Pediatr Oncol*. 2000; 35(2):91–95. [PubMed: 10918229]
- Skoczen S, Tomasiak PJ, Bik-Multanowski M, Surmiak M, Balwierz W, Pietrzyk JJ, Strojny W. Plasma levels of leptin and soluble leptin receptor and polymorphisms of leptin gene –18G > A and leptin receptor genes K109R and Q223R, in survivors of childhood acute lymphoblastic leukemia. *J Exp Clin Cancer Res*. 2011; 30:64.10.1186/1756-9966-30-64 [PubMed: 21631924]
- Skolin I, Wahlin YB, Broman DA, Koivisto Hursti UK, Vikstrom Larsson M, Hernell O. Altered food intake and taste perception in children with cancer after start of chemotherapy: perspectives of children, parents and nurses. *Support Care Cancer*. 2006; 14(4):369–378.10.1007/s00520-005-0904-6 [PubMed: 16633841]
- von Deneen KM, Liu Y. Obesity as an addiction: Why do the obese eat more? *Maturitas*. 2011; 68(4): 342–345.10.1016/j.maturitas.2011.01.018 [PubMed: 21376484]
- Weingarten HP, Elston D. The phenomenology of food cravings. *Appetite*. 1990; 15(3):231–246. [PubMed: 2281953]
- White MA, Grilo CM. Psychometric properties of the Food Craving Inventory among obese patients with binge eating disorder. *Eat Behav*. 2005; 6(3):239–245.10.1016/j.eatbeh.2005.01.001 [PubMed: 15854870]
- White MA, Whisenhunt BL, Williamson DA, Greenway FL, Netemeyer RG. Development and validation of the food-craving inventory. *Obes Res*. 2002; 10(2):107–114.10.1038/oby.2002.17 [PubMed: 11836456]
- Yu JH, Shin MS, Kim DJ, Lee JR, Yoon SY, Kim SG, Kim MS. Enhanced carbohydrate craving in patients with poorly controlled Type 2 diabetes mellitus. *Diabet Med*. 2013; 30(9):1080–1086.10.1111/dme.12209 [PubMed: 23586900]
- Zhang FF, Kelly MJ, Saltzman E, Must A, Roberts SB, Parsons SK. Obesity in Pediatric ALL Survivors: A Meta-Analysis. *Pediatrics*. 2014; 133(3):704–715.10.1542/peds.2008-1536
- Zhang FF, Liu S, Chung M, Kelly MJ. Growth patterns during and after treatment in patients with pediatric ALL: A meta-analysis. *Pediatr Blood Cancer*. 201510.1002/pbc.25519
- Zhang FF, Roberts SB, Parsons SK, Must A, Kelly MJ, Wong WW, Saltzman E. Low Levels of Energy Expenditure in Childhood Cancer Survivors: Implications for Obesity Prevention. *J Pediatr Hematol Oncol*. 201410.1097/mpb.0000000000000250
- Zhang FF, Rodday AM, Kelly MJ, Must A, Macpherson C, Roberts SB, Parsons SK. Predictors of being overweight or obese in survivors of pediatric acute lymphoblastic leukemia (ALL). *Pediatr Blood Cancer*. 2014; 61(7):1263–1269.10.1002/pbc.24960 [PubMed: 24482072]
- Zhang FF, Saltzman E, Kelly MJ, Liu S, Must A, Parsons SK, Roberts SB. Comparison of childhood cancer survivors’ nutritional intake with US dietary guidelines. *Pediatr Blood Cancer*. 201510.1002/pbc.25521

Highlights

- Childhood cancer survivors reported highest craving for fast-foods.
- Childhood cancer survivors diagnosed at an older age reported more food cravings.
- Food craving was not significantly associated with weight gain over 12 months.

Figure 1. Longitudinal trends in food craving in childhood cancer survivors

Food craving in childhood cancer survivors was assessed using a modified Food Craving Inventory. For total craving and craving for each subscale/component, the minimum score is 1 and the maximum scores is 5, with higher scores corresponding to higher frequency of craving. The means (standard deviations) of craving scores for total craving, and craving for fast-foods, carbohydrates, and fats are presented at baseline, 6 months, and 12-months. Longitudinal trends in all craving score over 12 months were not statistically significant (all P values > 0.05).

Table 1

Characteristics of childhood cancer survivors, the Healthy Living Study, 2011–2012

Characteristics	N=22
Age at study enrollment, <i>years</i> , median (Q1, Q3)	11.7 (7.5, 19.5)
Gender, N (%)	
Male	15 (68.2)
Female	7 (31.8)
Race/ethnicity, N (%)	
Non-Hispanic white	17 (77.3)
Other	5 (22.7)
Diagnosis	
Acute lymphoblastic leukemia	17 (77.3)
Hodgkin's lymphoma	3 (13.6)
Non-Hodgkin's lymphoma	2 (9.1)
Treatment status, N (%)	
On-treatment	3 (13.6)
Off-treatment	19 (86.4)
Age at diagnosis, <i>years</i> , median (Q1, Q3)	4.9 (3.0, 7.0)
Years since diagnosis, median (Q1, Q3)	5.6 (2.8, 8.3)
Body Mass Index (BMI) z-score, mean (SD)	0.8 (1.0)
Weight status, N (%) ^I	
Healthy weight	13 (59.1)
Overweight/obese	9 (40.9)

^I Weight status was defined as healthy weight if BMI z-score = −1.645–1.035 (or BMI =5th–84.9th percentile), overweight if BMI z-score =1.036–1.644 (or BMI=85th–94.9th percentile), and obese if BMI z-score ≥ 1.645 (or BMI ≥ 95th percentile) based on the current recommendations of the US Center for Disease Prevention and Control (CDC).

Table 2

Food craving by characteristics of childhood cancer survivors

	Total Craving			Fast-Foods			Sweets			Carbohydrates			Fats		
	N	Mean (SD)	β (95% CI) ³	Mean (SD)	β (95% CI) ³	Mean (SD)	β (95% CI) ³	Mean (SD)	β (95% CI) ³	Mean (SD)	β (95% CI) ³	Mean (SD)	β (95% CI) ³	Mean (SD)	β (95% CI) ³
Age at enrollment, <i>years</i>															
< 12.0	11	2.00 (0.67)	ref.	2.36 (0.95)	ref.	1.97 (0.75)	ref.	1.99 (0.65)	ref.	1.67 (0.64)	ref.	1.67 (0.64)	ref.		
12.0	11	2.25 (0.68)	0.002 (−0.48, 0.49)	2.77 (0.90)	0.30 (−0.42, 1.02)	2.31 (0.88)	0.11 (−0.63, 0.85)	2.08 (0.57)	−0.17 (−0.67, 0.33)	1.84 (0.70)	−0.23 (−0.82, 0.36)	1.84 (0.70)	−0.23 (−0.82, 0.36)		
Sex															
Male	15	2.17 (0.67)	ref.	2.67 (0.89)	ref.	2.21 (0.85)	ref.	2.08 (0.60)	ref.	1.73 (0.67)	ref.	1.73 (0.67)	ref.		
Female	7	2.02 (0.71)	−0.18 (−1.77, 0.41)	2.36 (1.05)	−0.29 (−1.17, 0.59)	1.98 (0.79)	−0.17 (−1.07, 0.74)	1.95 (0.63)	−0.16 (−0.77, 0.45)	1.80 (0.69)	−0.12 (−0.84, 0.60)	1.80 (0.69)	−0.12 (−0.84, 0.60)		
Age at diagnosis, <i>years</i>															
< 4.5	10	1.73 (0.57)	ref.	2.13 (0.94)	ref.	1.75 (0.76)	ref.	1.73 (0.52)	ref.	1.32 (0.32)	ref.	1.32 (0.32)	ref.		
4.5	12	2.45 (0.59)	0.88 (0.42, 1.34)	2.94 (0.78)	0.97 (0.29, 1.65)	2.46 (0.75)	0.96 (0.26, 1.66)	2.29 (0.54)	0.73 (0.25, 1.20)	2.11 (0.66)	0.87 (0.31, 1.43)	2.11 (0.66)	0.87 (0.31, 1.43)		
Treatment status															
Off -treatment	19	2.04 (0.65)	ref.	2.49 (0.97)	ref.	2.05 (0.79)	ref.	1.96 (0.59)	ref.	1.65 (0.56)	ref.	1.65 (0.56)	ref.		
On -treatment	3	2.67 (0.66)	0.44 (−0.30, 1.18)	3.08 (0.38)	0.53 (−0.57, 1.63)	2.67 (0.94)	0.55 (−0.58, 1.68)	2.50 (0.45)	0.32 (−0.45, 1.09)	2.42 (1.00)	0.36 (−0.54, 1.26)	2.42 (1.00)	0.36 (−0.54, 1.26)		
Cranial irradiation therapy															
No	20	2.17 (0.66)	ref.	2.63 (0.90)	ref.	2.21 (0.81)	ref.	2.07 (0.60)	ref.	1.78 (0.67)	ref.	1.78 (0.67)	ref.		
Yes	2	1.66 (0.84)	−1.07 (−1.79, −0.34)	2.00 (1.41)	−1.65 (−2.73, −0.57)	1.44 (0.62)	−1.31 (−2.42, −0.20)	1.69 (0.62)	−0.88 (−1.63, −0.13)	1.50 (0.71)	−0.43 (−1.31, 0.45)	1.50 (0.71)	−0.43 (−1.31, 0.45)		
Cumulative steroid doses (prednisone equivalents) ¹ , <i>mg/m²</i>															
Low (<4,000)	11	2.04 (0.68)	ref.	2.48 (0.98)	ref.	2.01 (0.79)	ref.	1.98 (0.63)	ref.	1.69 (0.53)	ref.	1.69 (0.53)	ref.		
High (≥ 4,000)	11	2.21 (0.69)	−0.005 (−0.44, 0.43)	2.66 (0.92)	−0.08 (−0.73, 0.56)	2.26 (0.87)	0.17 (−0.49, 0.83)	2.09 (0.58)	−0.01 (−0.46, 0.43)	1.82 (0.79)	−0.09 (−0.61, 0.44)	1.82 (0.79)	−0.09 (−0.61, 0.44)		
Weight status at enrollment ²															
Healthy weight	14	2.11 (0.82)	ref.	2.46 (1.04)	ref.	2.10 (0.94)	ref.	2.03 (0.71)	ref.	1.87 (0.79)	ref.	1.87 (0.79)	ref.		
Overweight/obese	8	2.14 (0.43)	0.30 (−0.27, 0.88)	2.72 (0.79)	0.72 (−0.14, 1.58)	2.19 (0.66)	0.48 (−0.41, 1.36)	2.04 (0.41)	0.14 (−0.46, 0.74)	1.60 (0.40)	−0.09 (−0.61, 0.44)	1.60 (0.40)	−0.09 (−0.61, 0.44)		

¹ Cumulative steroid doses were categorized into low and high based on median (i.e., 4000 mg/m²).

² Weight status was defined as healthy weight if BMI z-score = −1.645–1.035 (or BMI =5th–84.9th percentile), overweight if BMI z-score =1.036–1.644 (or BMI=85th–94.9th percentile), and obese if BMI z-score = 1.645 (or BMI ≥ 95th percentile) based on the current recommendations of the US Center for Disease Prevention and Control (CDC).

³ βs and 95% confidence intervals were adjusted for age at enrollment, sex, age at diagnosis, treatment status, receipt of cranial irradiation therapy, weight status at enrollment, and cumulative steroid dose (prednisone equivalents). Significant associations were bolded.

Table 3Repeated measures models^{*I*} on food craving and weight gain in childhood cancer survivors

Food Craving	Change in BMI z-score from baseline to 6 months	Change in BMI z-score from 6 months to 12 months
	β (95% CI) ^{<i>I</i>}	β (95% CI) ^{<i>I</i>}
Total	0.84 (−0.73, 2.41)	0.82 (−0.74, 2.39)
Fast-Foods	0.48 (−0.51, 1.47)	0.46 (−0.52, 1.45)
Sweets	0.67 (−0.50, 1.85)	0.66 (−0.51, 1.83)
Carbohydrates	0.90 (−0.84, 2.64)	0.90 (−0.82, 2.63)
Fat	0.21 (−1.54, 1.97)	0.21 (−1.54, 1.95)

^{*I*} β s and 95% confidence intervals were adjusted for age at diagnosis and receipt of cranial irradiation therapy.