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Depressive symptoms and physical activity among young adult survivors of childhood cancer

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Abstract

Objective: Young adult survivors of childhood cancers are less likely to be physically active compared to non-cancer affected controls, putting them at an increased risk for morbidity and mortality. Preliminary research has examined how mental health may contribute to physical activity (PA) in this population; however, those more recently diagnosed and Hispanic survivors have been understudied. The objectives were to examine associations of dimensions of depressive symptoms, demographic characteristics, and cancer-related predictors with PA among a diverse sample of young adult childhood cancer survivors.

Methods: Participants (N=895) diagnosed with childhood cancer between 1996–2010 (53% Hispanic; $M_{age}=26.2 \pm 4.9$ years; $M_{age}=14.8 \pm 4.4$ years at diagnosis) were recruited from the Los Angeles County cancer registry. Self-report surveys assessed current PA, depressive symptoms (i.e., positive affect, negative affect, somatic symptoms, interpersonal problems), late effects of cancer treatment, and demographic factors. Multivariable ordinal regressions examined the study objectives.

Results: About 70% of participants engaged in low or moderate frequency PA (fewer than 3 days a week). Participants who were older, female, Asian, or reported more late effects of cancer treatment were less likely to engage in PA. Greater positive affect was significantly associated with higher frequency PA, whereas negative affect, somatic symptoms, and interpersonal problems were not associated with PA.

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Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Author Contributions

BD: Writing- Original draft preparation, Formal Analysis, Writing – Reviewing & Editing. KAM: Conceptualization, Formal Analysis, Supervision, Writing – Reviewing & Editing. GFD: Writing – Reviewing & Editing. JEM: Conceptualization, Methodology, Supervision, Funding Acquisition, Writing – Reviewing & Editing.

Conclusions: The findings suggests that positive—but not negative—mental health characteristics are more likely to facilitate or result from PA among young adult survivors of childhood cancers. Interventions seeking to increase PA may benefit from considering positive aspects of mental health/well-being.

Keywords

cancer; mental health; oncology; physical activity; young adult

Introduction

Young adult survivors of childhood cancer experience unique health challenges, such as being at an increased risk for obesity, diabetes, osteoporosis, and cardiovascular disease^{1–3}. Despite improvements in treatment regimens resulting in over 80% five-year survival rates, the majority of childhood cancer survivors experience late adverse effects (e.g., second malignancies, psychosocial problems) that become apparent years after treatment ends⁴. It estimated that 95–99% of childhood cancer survivors will have chronic health conditions (e.g., hypertension, endometriosis, arthritis) related to their cancer therapy, such as by the age of 50⁵. Furthermore, childhood cancer survivors are eight times as likely to die prematurely compared to age- and gender-matched peers⁶. Therefore, it is recommended that survivors practice health-promoting behaviors in order to reduce their risk for negative health outcomes such as chronic diseases, cancer recurrence, secondary cancer, mortality, and late-effects related to their diagnoses and treatment^{7,8}. Modifiable health behaviors, such as physical activity (PA), may mitigate these health consequences and maximize long-term health throughout adulthood.

Over the past decade, a substantial accumulation of evidence indicates that low PA is associated with the occurrence of several types of cancers and PA may improve long-term survival for those diagnosed with cancer^{8–10}. PA can prevent an array of chronic conditions such as obesity, Type II diabetes, and cardiovascular disease^{11,12} among cancer and non-cancer affected populations. In addition, PA can play a preventive role in some cancers such as colon, breast, and endometrial among the general adult population^{13,14}. PA after cancer diagnoses may reduce the risk of cancer recurrence, cancer-specific mortality, and overall mortality^{8–10}. The Physical Activity Guidelines for Americans recommend that adults—even those with chronic conditions such as cancer—engage in at least 150 minutes of moderate-to-vigorous PA a week for health benefits¹⁵. However, only 10% of young adults in the United States meet the national PA recommendations, putting them at greater risk for negative health outcomes¹⁶. Young adult survivors of childhood cancer are less likely to meet general PA recommendations compared to non-cancer affected controls^{17,18}. Increasing PA among young adult survivors—a unique population at risk for inactivity and health consequences related to cancer diagnoses and treatment—is necessary to ensure healthy outcomes for this at-risk population.

To promote PA among young adult survivors, elucidating determinants of regular PA is necessary. Previous research has examined associations between psychological variables and PA among young adult survivors of childhood cancer. Depression^{19,20} and emotional

discomfort²¹ were inversely associated with PA. While these studies provide evidence for associations between mental health and PA in cancer survivors, there are some limitations in the literature. First, many PA studies conducted among young adult survivors use convenience samples from health clinics that are majority non-Hispanic White. Given the growing racial and ethnic diversity of young adults living in the United States (e.g., 19% and 7% of Americans identify as Hispanic or Asian, respectively), more research among diverse samples is needed to understand these relationships among different populations. Epidemiological evidence indicates Latino adults have a higher prevalence of depressive symptoms compared to their non-Latino counterparts, and it has been proposed that ethnicity may be a moderator in the PA and depression relationship²². Second, many studies utilize data from the Childhood Cancer Survivor Study; while this is a very large cohort of young adult survivors, participants were diagnosed between 1970–1999. PA patterns among those more recently diagnosed/treated is less understood, and additional research is warranted given overall decreases in activity among adults. Lastly, studies have yet to investigate the influential role of individual dimensions of depression. Depression is a complex set of features involving different intermediate phenotypes (e.g., anhedonia, somatic symptoms) rather than a unitary homogenous syndrome^{23,24}; therefore, exploring whether different dimensions are associated with PA can provide a nuanced understanding of mental and physical well-being. Examining whether particular dimensions of depression are associated with PA can help determine which psychological characteristics may be greater risk/protective factors as well as potential targets for future interventions. Cox and colleagues reported negative affect significantly explained variance in PA engagement among young adult survivors, but the potential influential role of positive affect on PA has yet to be studied among this group²⁵. Given the high rates of depressive symptoms among childhood cancer survivors²⁶, elucidating associations between depression and PA is critical.

To address gaps in the literature and add to the growing number of studies on PA among young adult childhood cancer survivors, the main objective the study was to examine the associations between dimensions of depressive symptoms and PA among a racially and ethnically diverse cohort of young adults diagnosed with childhood cancer between 1996–2010. The secondary objective was to examine demographic and cancer-related predictors of PA. We separately examined each dimension of the Center for Epidemiologic Studies Depression Scale (CES-D): positive affect, negative affect, somatic complaints, interpersonal problems²⁷. The current study, an exploratory secondary analysis, utilizes data from Project Forward, a diverse, cancer registry-derived population-based cohort of young adult survivors (19–39 years old at survey).

Methods

Participants

Participants ($N=895$) included young adult survivors of childhood cancer from the Project Forward Study, a cross-sectional population-based cohort study examining follow-up care among young adults diagnosed with any type of cancer (stage 2 or greater, except for brain and melanoma, which included stage 1 or greater) in Los Angeles County between 1996 and 2010²⁸. Participants were diagnosed between the ages of 0 and 19, five or more years

from diagnosis, and between the age of 18 and 39 when the study began in 2015. Study participants were identified through the Los Angeles Cancer Surveillance Program, the Surveillance, Epidemiology, and End Results (SEER) Cancer Registry covering Los Angeles County.

Procedures

Eligible participants were mailed a paper survey to complete. Surveys were available in both English and Spanish and were available online. To increase recruitment efforts and achieve a representative sample, the Dillman Survey Method was used, which utilizes multiple methods to locate and recruit participants (e.g., telephone follow-up, mailing surveys, mailing postcard reminders, providing a telephone interview option)²⁹. Upon completing the survey, participants were compensated with a \$20 gift card and an entry to a lottery to win \$300. Informed consent was obtained, and all study procedures were approved by the California Committee for the Protection of Human Subjects of the California Cancer Registry and the Institutional Review Board at the University of Southern California (HS-14-00817). Full study procedures are detailed elsewhere²⁸.

Measures

Depressive Symptoms—Depressive symptoms were assessed through the self-report Center for Epidemiologic Studies Depression Scale (CES-D)²⁷. The CES-D is a scale commonly used to evaluate current depressive symptom severity and has shown high diagnostic accuracy in adults, but is not a diagnostic measure. The 20-item scale assessed the frequency of depressive symptoms in the past week with response items ranging from “Rarely/none of the time” to “Most or all of the time”. The four subscales (dimensions) of the CES-D, which represent depressive symptoms, were examined in the current study: positive affect (i.e., low positive affect), negative affect (i.e., depressed affect), somatic complaints (i.e., my sleep was restless), and interpersonal problems (i.e., people were unfriendly). Sample items include: “I was happy” (positive affect), “I was bothered by things that usually don’t bother me” (negative affect), “I felt like everything I did was an effort” (somatic complaints), and “I felt that people dislike me” (interpersonal problems). Scores for each subscale were summed, respectively. Scores can range from 0–60, with higher scores indicating more severe symptoms and a cutoff score of 16 used to identify individuals at risk for clinical depression.

Physical Activity Frequency—Participants were asked the following item which was adapted from the Godin Leisure-Time Exercise Questionnaire: “Considering a 7-day period (a week), how often do you engage in any regular activity long enough to work up a sweat (**heart beats** rapidly)?”³⁰. The original questionnaire has shown good validity among cancer-affected populations³¹. Response options included “Never (0 days)”, “Rarely (1 day)”, “Sometimes (2–3 days)”, “Often (4–5 days)”, and “Very often (6–7 days)”. For the current analysis, responses were categorized into the following three categories: low frequency (Never and Rarely), medium frequency (Sometimes), and high frequency (Often and Very Often).

Demographic and Clinical Characteristics—Age at diagnosis, age at survey completion, sex (female, male), race/ethnicity (non-Hispanic White, Hispanic, Asian, Other), cancer diagnosis (site/histology), and years since diagnosis were obtained from the cancer registry. Quintiles of socioeconomic status (SES) at diagnosis were also obtained from the cancer registry; the quintile variable (1=lowest quintile and 5=highest quintile) is a census-based composite score relative to California’s statewide distribution reflecting seven indicators (e.g., education index, percent persons above 200% poverty line, median household income)^{32,33}. Treatment intensity was calculated using cancer registry data as a proxy of medical chart data; values for treatment intensity ranged from 1=least intensive (e.g., surgery only) to 4=most intensive (e.g., relapse regimens)²⁸. Self-reported late effects of cancer treatment were assessed by 11 items (e.g., heart problems, putting on weight, lung problems/difficulty breathing). The items were selected based on the most prevalent chronic conditions previously reported among childhood cancer survivors⁴. Summary scores were calculated and categorized as none, one, or two or more late effects.

Statistical Analysis

Descriptive means and frequencies were used to describe the study sample. Multi-variable ordinal regression analysis examined whether the four subscales of the CES-D—positive affect, negative affect, somatic complaints, interpersonal problems—were uniquely associated with engaging in PA (i.e., high frequency, medium frequency, low frequency). All four subscales were added as predictors a priori. The final model was weighted to account for survey response bias (e.g., correcting for differences in the distribution of sex, race/ethnicity, and SES between survey responders and non-responders). The model controlled for current age, sex, race/ethnicity, SES, treatment intensity, and number of late effects. Statistical significance was set at $p < .05$. Odds ratios (OR), adjusted odds ratios (AOR), and 95% confidence intervals (CI) are reported. All analyses were conducted using SAS statistical software (Version 9.4).

Results

Participant Characteristics

There were 2,788 eligible participants. A total of 196 were subsequently deemed ineligible, and another 1,426 were not enrolled (e.g., declined to participate, loss of contact), resulting in 1,166 participants enrolled in the study. Participants ($n=60$) reported a treatment in the prior two years and were excluded from the analyses, resulting in a sample of 1,106. A total of 211 participants were further excluded for having missing data on variables of interest. The final analytic sample was $N=895$.

Descriptive statistics for the demographic characteristics of the analytical sample are presented in Table 1. Participant ranged in age from 18–41 years with an average age of 26.21 ($SD=4.88$) years at the time of survey completion. Half of the sample was female and 53% identified as Hispanic. Descriptive statistics for self-reported PA are also shown in Table 1. Regarding depressive symptoms, the mean positive affect was 8.44 ($SD=2.93$; range: 0–12), the mean negative affect score was 4.24 ($SD=4.72$; range: 0–21), the mean interpersonal problems score was 0.84 ($SD=1.31$; range: 0–6), and the mean somatic

complaints score was 4.71 (SD=3.47; range: 0–18). The mean composite CES-D score was 13.88 (SD=10.91, range 0–58) and about 33.6% of the sample were considered individuals at risk for clinical depression (i.e., CES-D scores greater than 16).

Among the larger study sample (n=2592), responders to the survey (vs. non-responders) were more likely to be female (vs. male) ($\chi^2=23.39$, $p<.05$), non-Hispanic White ($\chi^2=29.68$, $p<.05$), and have higher (vs. lower) socioeconomic status ($\chi^2=15.67$, $p<.05$)²⁸.

Results of the multivariable ordinal regression analysis are shown in Table 2. Participants who were older, female, Asian, or reported more late effects engaged in PA less frequently. For a one-unit increase in current age, the odds of high frequency PA were 0.96 times lower than for the combined effect of middle and low frequency PA (OR=0.96, 95% CI [0.94, 0.97]). Females (vs. males) were half as likely (OR=0.50, 95% CI [0.37, 0.67]) to have a one-unit change in PA frequency. In addition, Asian participants, compared to Non-Hispanic White participants, were about half as likely (OR=0.48, 95% CI [0.31, 0.76]) to have a one-unit change in PA frequency. Participants with one (OR=0.56, 95% CI [0.41, 0.77]) or two or more (OR=0.63, 95% CI [0.52, 0.77]) late effects, compared to participants with zero late effects, were less likely to have a one-unit change in PA frequency. Socioeconomic status at diagnosis was associated with PA frequency (medium SES OR=1.52, 95% CI [1.08, 2.15]; highest SES OR=1.57, 95% CI [1.02, 2.43]).

Associations Between Depressive Symptoms (CES-D subscales) and PA Frequency

Unadjusted models—without covariates age, sex, SES, treatment intensity, and number of late effects—indicated the association between positive affect and PA was significant (OR=1.07, $p<.05$), whereas the three other depressive symptom subscales (i.e., negative affect, interpersonal problems, somatic problems) were not significantly associated with PA ($ps>.05$).

The results of the multivariable ordinal regression analysis are also shown in Table 2. Of the four CES-D subscales for depressive symptoms, only positive affect was significantly associated with PA frequency. For a one-unit increase in positive affect, the odds of high frequency PA versus the combined effect of medium and low frequency PA was 1.10 times greater (OR=1.10, 95% CI [1.04, 1.16]). The odds of PA frequency were not associated with negative affect, interpersonal problems, or somatic complaints ($ps>.05$).

Discussion

To our knowledge, the current study is one of the first to examine associations between different dimensions of depression (i.e., positive affect, negative affect, somatic symptoms, and interpersonal problems) and PA among a majority Hispanic sample of young adult survivors of childhood cancer. The study had several strengths, such as including an ethnically diverse, population-based sample of young adult survivors with population weights. Results indicated young adult survivors who report greater positive affect engaged in more PA, whereas negative affect, somatic symptoms, and interpersonal problems were not significantly associated with PA frequency. The findings suggests positive—but not negative—mental health characteristics may be more likely to facilitate PA or result from

PA among cancer survivors. These findings add to the limited literature on psychological correlates of PA among young adult survivors of childhood cancer survivors.

Results of this study indicated positive affect was associated with greater PA frequency (i.e., 4–7 days versus less than 4 days per week) such that for a one-unit increase in positive affect, the odds of high frequency PA versus the combined effect of medium and low frequency PA were 1.10 times greater. These findings are in line with the extant literature among the general adult population, such that there are bi-directional associations between positive affect and negative affect with PA³⁴. Among adults who have been diagnosed with cancer, empirical research has largely assessed the associations between quality of life—which encompasses psychological, social, physical, and functional aspects/limitations of well-being—and PA; evidence suggests positive associations between quality of life and PA^{35,36}. Our findings, taken together with prior evidence regarding positive affect and PA, suggest longitudinal research is needed to investigate these associations over time to assess whether positive affect facilitates increased PA frequency, whether positive affect is a result of PA engagement, or if there are dynamic bidirectional associations. In addition, future research could examine whether PA is potentially a mediator for health-related quality of life.

Negative affect, somatic symptoms, and interpersonal problems were not associated with PA frequency in the study sample. These findings extend previous research among cancer survivors, which has reported depression being associated with less PA^{19,20}. The inconsistent findings may be due to most research utilizing a composite score to assess depression, versus disaggregating the measures and examining associations with dimensions. Depression is a dynamic condition with distinct dimensions that can impact individuals and their behaviors differently²⁴. About 33% of the study sample met the clinical cut off for being at risk for depression, which is higher than the prevalence of depression among the general population. However, the CES-D is considered a screening tool, not a diagnostic tool; the associations between negative affect, somatic symptoms, and interpersonal problems with PA may differ among samples with clinically diagnosed depression. Overall, the study findings underscore the importance of investigating different dimensions of depressive symptoms given that distinct dimensions may uniquely explain the mechanisms underlying the depression and PA association. Future research should examine the unique associations of PA and the multiple dimensions of depression in additional diverse study samples and in the context of PA interventions. PA programming may be more effective at long-term behavior change if they are able to adequately address these distinct dimensions of positive affect, negative affect, interpersonal problems, and somatic problems.

In addition to examining associations between depressive symptoms and PA, several demographic and clinical factors were examined in their relation to PA in the multivariable model. In line with previous research, female young adult survivors had lower odds of high PA frequency²¹. To our knowledge, the current study is one of the first to show that compared to White participants, Asian participants were less likely to be in the high frequency PA group. These findings are in line with prior research among the general Asian American population, which indicates that those who identify as Asian are less likely to engage in PA compared to other racial/ethnic groups³⁷. Prior PA levels are strong predictors

of PA post-cancer diagnosis across all racial and ethnic groups; therefore, elucidating and addressing barriers to PA engagement among Asian Americans may have positive short- and long-term effects^{38,39}. Understanding demographic characteristics associated with PA among young adult survivors, along with the possible underlying relationships, may inform public health and health care efforts. Study findings also indicated late effects were associated with PA: participants with one or more late effects (vs. zero late effects) were less likely to be in the high frequency PA group. Findings are in line with previous studies; late effects are associated with both inactivity and poor physical performance¹⁹. Healthcare providers and public health messaging geared towards young adult survivors should highlight engaging in regular PA can help reduce the severity of late effects and other diseases.

Limitations

There are some limitations to note. The single item measure for PA is not ideal, and capturing objective PA through activity trackers is recommended. In addition, the item used in the current study has not yet been validated among young adult survivors; the one item was used for brevity and was adapted to capture overall strenuous PA. Furthermore, duration and intensity of PA was not assessed, limiting the possibility to determine if participants met the national recommendations for optimal health. While the current study extends previous research by including a large proportion of Hispanic participants, it is important to note the findings may not be generalizable to the larger population of survivors, such as non-Hispanic Black young adults given the small sample size. Responders to the survey (vs. non-responders) were more likely to be female, non-Hispanic White, and have higher SES, and this responder bias may have influenced the results given associations between sociodemographic characteristics and PA. This was also a general sample, and not those with clinical depression. Lastly, considering conclusions on causality between depressive symptoms and PA frequency cannot be made, future longitudinal research is needed to elucidate the effects of depressive symptoms on PA—and vice versa—among this sample in order to test the potential effects of future interventions and provide clinical recommendations.

Clinical Implications

By gathering more information on the psychological correlates of PA, such as distinct dimensions of depressive symptoms, exercise intervention studies and health promotion efforts from health care providers can be better adapted to young adults. In addition, the assessment of different dimensions of depressive symptoms may be used to identify who may be less likely to engage in sufficient levels of PA. Future clinical research could examine whether positive affect moderates the effects of PA interventions among young adult survivors. Furthermore, clinical programs may benefit from considering and incorporating other psychosocial correlates and positive aspects of mental health/well-being such as resiliency or post-traumatic growth³⁸.

Conclusion

Overall, the study findings indicate that positive, rather than negative mental health, characteristics are more likely to facilitate or result from PA among young adult survivors of childhood cancers. These findings contribute to the growing literature examining PA among young adult survivors by including a sample that is more ethnically diverse and more recently diagnosed. Interventions aiming to promote PA among survivors of childhood cancer may benefit from considering positive aspects of mental health/well-being.

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Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Table 1

Participant Characteristics (N=895)

Demographics	n (%)
Age at survey completion (Mean ± SD)	26.21 ± 4.88
Age at diagnosis (Mean ± SD)	11.74 ± 5.34
Years since diagnosis (Mean ± SD)	14.47 ± 4.38
Sex	
Female	451 (50.39)
Male	444 (39.61)
Race/Ethnicity	
Asian	89 (9.94)
Hispanic	481 (53.74)
Other	83 (9.27)
Non-Hispanic White	242 (27.04)
Socioeconomic status at diagnosis	
Lowest	219 (24.47)
Low	173 (19.33)
Medium	175 (19.55)
High	166 (18.55)
Highest	162 (18.10)
Treatment Intensity[†]	
1 (least intensive)	59 (6.59)
2 (moderately intensive)	277 (30.95)
3 (very intensive)	431 (48.16)
4 (most intensive)	128 (14.30)
PA Frequency	
Low	278 (31.06)
Medium	353 (39.44)
High	264 (29.50)

[†]Intensity of Treatment Rating (based on both registry and self-report data, see Methods)

Table 2

Multivariable ordinal logistic regression model of physical activity frequency among childhood cancer survivors (N=895)

	Estimate (<i>SE</i> [†])	Adjusted OR [‡]	Adjusted OR 95% CI [§]
Age at survey completion	-0.04 (0.01)	0.96**	0.94, 0.97
Sex (Female)	-0.70 (0.15)	0.50***	0.37, 0.67
Race (Reference group: Non-Hispanic White)			
Asian	-0.73 (0.23)	0.48**	0.31, 0.76
Hispanic	-0.02 (0.14)	0.97	0.74, 1.28
Other	-0.22 (0.25)	0.80	0.49, 1.32
Socioeconomic status at diagnosis (Reference group: Lowest quintile)			
Low	0.10 (0.23)	1.11	0.70, 1.77
Medium	0.42 (0.17)	1.52*	1.08, 2.15
High	0.54 (0.28)	1.72	0.98, 3.01
Highest	0.45 (0.22)	1.57*	1.02, 2.43
Treatment intensity (lowest to highest)	0.06 (0.07)	1.06	0.92, 1.22
Number of late effects (Reference group: None)			
One	-0.58 (0.16)	0.56***	0.41, 0.77
Two or more	-0.46 (0.10)	0.63***	0.52, 0.77
Years since diagnosis	0.01 (0.02)	1.01	0.97, 1.05
Positive affect	0.10 (0.03)	1.10**	1.04, 1.16
Negative affect	0.01 (0.03)	1.01	0.95, 1.06
Interpersonal problems	0.06 (0.05)	1.06	0.96, 1.17
Somatic complains	-0.003 (0.02)	0.99	0.95, 1.04

* $p < .05$,

** $p < .01$.,

*** $p < .001$

[†]SE=Standard Error.

[‡]OR= Odds Ratio.

[§]CI = Confidence Interval

For the dependent variable, the reference group is high frequency PA (i.e., 4–7 days).