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Relations between Posttraumatic Stress and Posttraumatic Growth in Long-Term Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study

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Abstract

Objective—Contemporary models of trauma suggest that posttraumatic stress and growth should be related, and that symptoms of stress resulting from a perceived trauma (e.g. childhood cancer) are prerequisite for posttraumatic growth to occur. However, empirical data regarding the relationship of posttraumatic stress and growth have been equivocal. The purpose of this study is to examine the relationship between posttraumatic stress symptoms (PTSS) and posttraumatic growth (PTG) among adult survivors of childhood cancer.

Methods—Survey methods were utilized to collect data from 6162 survivors participating in the Childhood Cancer Survivor Study (CCSS). Non-parametric correlation was examined pair-wise between PTG and PTSS using Spearman's correlation coefficient with 95% confidence intervals, with non-linear canonical correlation analysis being conducted to examine relationships between subscales. A multivariable partial proportional odds model was also fit for PTG Total quartiles focusing on associations with PTSS Total quartiles while adjusting for sociodemographic and medical variables.

Results—Examination of unadjusted PTSS and PTG total scores revealed a Spearman correlation of 0.11 ($p<0.001$), with coefficients ranging from 0.03 to 0.17 between total and subscale scores. The non-linear canonical correlation analyses resulted in two Dimensions with Eigenvalues of 0.15 and 0.14, resulting in a fit value of 0.30 and evidence that little variability in the data (15%) was explained by the weighted combinations of the variables.

Conclusions—Although statistically significant, these results do not indicate a robust relationship between PTSS and PTG among adult survivors of childhood cancer. Theories suggesting that PTSS is a prerequisite for PTG should be reconsidered.

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Being diagnosed and treated for pediatric cancer can be traumatic, and late effects of treatment exacerbate these symptoms (Wenninger et al., 2013). For survivors, the resulting trauma-induced stress may persist as posttraumatic stress symptoms (PTSS), or less frequently, posttraumatic stress disorder (PTSD). Although investigators have historically focused on describing PTSS among survivors, a developing literature is considering the personal growth resulting from cancer-related traumatic stress, often referred to as posttraumatic growth (PTG; Tedeschi & Calhoun, 1995). PTG refers to the positive changes resulting from the struggle with a traumatic event, and not to the changes caused by the event itself (Tedeschi & Calhoun, 2004). A construct closely related to PTG is that of benefit finding, which has often been used interchangeably (Carver & Antoni, 2004; Tomich & Helgeson, 2004).

Tedeschi and Calhoun's (2004) framework of posttraumatic growth posits that posttraumatic stress and growth are related. If there is PTG from a trauma, this growth must be preceded by stress resulting from that trauma. Theoretically, stress causes growth by challenging the individual's world view and precipitating a rethinking or reordering of priorities. The construct of PTG raises the question of whether growth after a perceived trauma is associated with trauma-related stress symptoms, or whether PTSS may persist and/or coexist with PTG.

Given the inherent challenges of utilizing longitudinal designs in the context of cancer diagnosis and treatment, few studies have addressed whether stress symptoms resulting from the trauma of cancer diagnosis and treatment are reduced in the presence of PTG. Carver and Antoni (2004) partially addressed this question by measuring benefit finding, but not PTSS, and found that initial benefit finding in women with early stage breast cancer was related to greater positive emotions and lowered depressive symptomatology four to seven years later. In contrast, Tomich and Helgeson (2004) measured benefit finding (along with positive and negative affect) in women surviving breast cancer and found that initial benefit finding was associated with greater negative affect and reductions in mental health over time for women with more advanced disease, as compared to those with early stage breast cancer.

Studies measuring PTSS and PTG simultaneously (as is the case in the presented study) have resulted in mixed findings, ranging from moderate positive to moderate negative correlations, which appear to be dependent on the population studied. In combat veterans and other war-related circumstances, a moderate negative relationship has been reported (Wood, Britt, Wright, Thomas, & Bliese, 2012). Studies of adult cancer survivors have reported correlations ranging from non-significant and near-zero to moderately positive (Koutrouli, Anagnostopoulos, & Potamianos, 2012; Morrill et al., 2008; Salsman, Segerstrom, Brechtin, Carlson, & Andrykowski, 2009). In other settings, a curvilinear (inverted-U) has been found (Kleim & Ehlers, 2009). Specific to survivors of childhood cancer, Barakat, Alderfer, and Kazak (2005) reported a moderate correlation ($r = 0.35$), whereas Phipps, Long and Ogden (2007) found a non-significant ($r = 0.00$) correlation. To date, most studies in the oncology setting have been limited by relatively small sample sizes.

The purpose of the current study is to examine the relationship between PTSS and PTG in a large sample of survivors from the Childhood Cancer Survivorship Study (CCSS), while

controlling for factors that may influence outcome including gender, age at enrollment, education, race/ethnicity, income, marital status, subsequent malignant neoplasm (SMN) or recurrence, and primary diagnosis. This study improves upon previously conducted research in this area in that it includes a large multi-institutional and geographically-diverse sample.

Methods

Participants

The CCSS is a longitudinal cohort study that tracks the health status of survivors of childhood cancer diagnosed between 1970 and 1986 and treated at one of 26 collaborating centers across the United States and Canada. The CCSS protocol and surveys completed by participants were reviewed and approved by institutional review boards at each participating center. Participants provided informed consent for study participation and for release of medical information. Detailed descriptions of the study design and characteristics of the cohort have been reported elsewhere (Robison, Armstrong, Boice, et al., 2009). Data considered were collected as part of the second CCSS follow-up survey (N=9308) which focused on, in part, psychological outcomes and health behaviors. The current study utilized data from 6162 of these participants after adjusting for those who received a shorter CCSS survey that excluded psychological measures (n=2268), and those who were <18 years of age or had the survey completed via proxy (n=878).

Survivors were, on average, 31.6 years (SD = 7.6) of age at survey completion (range = 18 – 53 years), 8.2 years (SD = 5.9) at diagnosis (range = 0 – 20 years), and 23.1 years (SD = 4.5) since diagnosis. Fifty-two percent were female, 87.8% self-identified as being non-Hispanic white, 84.9% were at least high school graduates, and 51.4% were married/living as married. See Supplemental Table 1 for more details. Compared to survivors who completed the baseline CCSS survey, follow-up survey participants were significantly more likely to be older, female, white, employed, married/partnered, and older age at diagnosis and fewer years since diagnosis (Stuber et al., 2010). Furthermore, survivor participants did not differ from non-participants by cancer diagnosis, survival time, or on a standardized measure of psychological distress assessed at baseline.

Measures

Posttraumatic Growth Inventory (PTGI; Tedeschi & Calhoun, 1996)—As the most widely used measure of growth/benefit following trauma in adults, the PTGI was used to assess PTG via a 21-item scale that is composed of 5 subscales (*Relating to Others, New Possibilities, Personal Strength, Spiritual Change, Appreciation for Life*), that when summed, generates the PTG total score. Wording of the question stem was modified from the original measure given that participants diagnosed at very young ages would not realistically be able to determine whether they had/had not experienced “change” as a result of having had cancer. Thus, the PTGI was adapted to assess the extent to which respondents believed they were *influenced* (as opposed to “changed”) by their cancer experience. Participants were directed to respond to each item, with response options provided on a six-point scale ranging from (0) “I am NOT influenced by my experience” to (5) “I am influenced to a VERY GREAT degree as a result of my experience.” As such, PTG total

scores range from 0 to 105, with higher scores suggesting greater PTG. The PTGI subscales are reported to have good internal reliability, with coefficient alphas in this study ranging from 0.84 – 0.86 for subscale and Total scores.

Posttraumatic Stress Diagnostic Scale (PSDS; Foa, Cashman, Jaycox, & Perry, 1997)—PTSS was measured with the PSDS, an instrument consisting of 17 items that produce 3 subscales (Re-experiencing, Avoidance, and Arousal) and a total PTSS severity score. Each item queries the respondent as to whether he/she has experienced a specific PTSD-associated symptom within the previous month, which the respondent then rates on a 4 point scale: (0) not at all or only 1 time, (1) once in a while, (2) one half of the time, and (3) almost always. As such, severity (or total) scores range from 0 to 51 with higher scores suggesting greater severity of PTSS symptoms. Because there was particular interest in studying PTSS as a function of childhood cancer, the instructions of the PSDS were modified and respondents were asked to rate each listed problem with respect to their childhood cancer experience. Despite this change, the internal reliability of this instrument remained robust with coefficients (Cronbach's alpha) for the PSDS Total and subscales ranging from 0.86 – 0.87.

Statistical approach

Descriptive statistics were calculated for the PTSS measures, PTG measure, demographic factors and treatment variables for the survivors. Non-parametric correlation was examined pair-wise between PTG (Total, Re-experiencing, Avoidance, and Arousal) and PTSS (Total, Relating to Others, New Possibilities, Personal Strength, Spiritual Change, Life Appreciation) using Spearman correlation coefficients, with associated 95% confidence intervals (CI) reported. Several approaches were used to assess associations between the measures. A partial proportional odds model was then fit for the ordinal outcome defined by PTG Total quartiles (scores of 0–33, 4–58, 59–75, 76–105), with key focus on assessing associations with quartiles of PTSS Total (scores of 0, 1–3, 4–8, 9–51), while adjusting for gender, age at enrollment, education, ethnicity or race, income, marital status, SMN or recurrence, and exposures to chemotherapy and radiation. During model fitting, the proportional odds assumption was tested (i.e., that risk factors exhibited a consistent odds ratio across each cut point of the outcome variable). Due to the finding of non-proportional odds for the association of age at diagnosis and PTSS Total score with the outcome, the model structure was relaxed so that these variables were permitted to have varying odds ratios across the outcome cut points, resulting in a partial proportional odds model. Multivariable odds ratios and associated 95% CI's are presented (Peterson & Harrell, 1990). Finally, a non-linear canonical correlation analysis was carried out to evaluate the relationships between the subscales for each set of measures. This approach is similar to a standard canonical correlation analysis except that simultaneous to looking for optimized weight matrices for combining the original variables, it also looks for optimal scaling of the variables. Variables were assumed to be ordinal for this analysis, and thus, transformations retained their ordering. This method is appropriate for the PTSS and PTG data, which was highly skewed and non-normally distributed (Van der Burg & De Leeuw, 1983). Most statistical analyses were performed with SAS Version 9.1 (SAS Institute Inc., Cary, NC, USA), using two-sided statistical inferences and a significance level of $p \leq 0.05$. The non-

linear canonical correlation analysis was carried out using the *homals* function in *R*, Version 3.0.2 (R Foundation for Statistical Computing, Vienna, Austria. http://www.R-project.org/).

Results

Over 71% of our sample reported some PTSS, and the mean Total Severity Score was 5.43 (SD=7.14), and the mean subtest scores were 1.06 (SD=1.89), 2.33 (SD=3.44), and 2.04 (SD=2.87) for Re-experiencing, Avoidance, and Arousal, respectively. The mean Total Score for PTG was 53.94 (SD=27.56), and is as follows for the following subscales: Relating to Others = 17.98 (SD=9.91), New Possibilities = 10.21 (SD=7.13), Personal Strength = 11.41 (SD=5.75), Spiritual Change = 4.99 (SD=3.60) and Life Appreciation = 9.34 (SD = 4.34).

Examination of the unadjusted PTSS and PTG total scores revealed a correlation of 0.11 (95% CI: 0.09, 0.14; $p<0.001$) suggesting a weak, but positive, relationship between these two constructs. When relationships among the rest of the pair-wise combinations of PTSS and PTG total and subscale scores were considered, coefficients ranged from 0.03 (95% CI: 0.009, 0.059) to 0.17 (95% CI: 0.14, 0.19). All correlations were significantly different from zero, but this is due to the very large sample size; interpretation should be placed on correlation estimates and confidence intervals. See Supplemental Table 2. The non-linear canonical correlation analyses resulted in two Dimensions with Eigenvalues of 0.15 and 0.14, and a fit value of 0.30, evidence that little of the variability in the data (15%) was explained by the weighted combinations of the variables. Variable loadings did not illustrate particularly high correlations between any of the optimally scaled subscores and the object scores (highest of 0.38 for PTS Re-experiencing). See Supplemental Figure 1.

In a multivariable partial proportional odds model, PTG quartile membership was associated with sociodemographic and cancer-specific variables, along with PTSS. For 9 of 12 final model variables, the proportional odds assumption was met, demonstrating a consistent association when moving between each of the PTG quartiles (Table 1). In terms of sociodemographic variables, females were 46% more likely than males to experienced increased PTG (OR 1.46, 95% CI 1.32–1.61), whereas non-white survivors were 23% more likely (OR 1.23, 95% CI 1.06–1.43) and those divorced/separated/widowed were 13% more likely (OR 1.13, 95% CI 1.00–1.27) to experience increases in PTG as compared to their single counterparts. In regard to cancer-specific variables, those survivors who experienced a SMN/recurrence were 62% more likely than those who had not, to experience increases in PTG (OR 1.62, 95% CI 1.42–1.85). Treatment also contributed to PTG in that those survivors with a history of receiving RT to an unknown site (as compared to those with no RT history), were 50% more likely to experience increased PTG, whereas those who received Anthracyclines/Alkylators (OR 1.70, 95% CI 1.50–1.93) or another type of chemotherapy (OR 1.28, 95% CI 1.09–1.51) were 70% and 28% more likely, respectively, to experience increased PTG as compared to those who experienced no chemotherapeutic exposures.

In contrast to the consistent association of variables at each PTG quartiles for the above variables, age at diagnosis and PTSS demonstrated non-proportional associations across

PTG quartiles (bottom of Table 1). Using survivors diagnosed between 0–4 years as the referent those diagnosed at ≥ 5 years were between 1.4–2.1 times more likely to report increases in PTG. Furthermore, those survivors with some PTSS (i.e. PTSS total score ≥ 1) were between 1.5 (2^{nd} PTSS quartile) to 2.2 times (4^{th} PTSS quartile) more likely to report PTG (95% CIs range from 1.29–2.58, p<.0001).

Discussion

The developers of the posttraumatic growth construct theorized that growth occurs in the context of posttraumatic stress, and therefore a positive relationship should exist between PTG and PTSS (Tedeschi & Calhoun, 1996; 2004). Others have argued that PTSS should relate negatively to growth, while others suggest they are independent constructs that have no systematic relationship (Linley & Joseph, 2004). The empiric data have been as divergent as these theoretical positions. In regards to health-related stressors, and cancer in particular, the empiric data have generally ranged from non-significant and near zero to moderately positive correlations, with little evidence of a negative relationship (Koutrouli et al., 2012; Morrill et al., 2008; Salsman et al., 2009). However, the samples in these studies have generally been small, rarely exceeding an N of 100. In contrast, the current study included a very large, heterogeneous and multisite sample of childhood cancer survivors that allows for control of demographic and medical variables. The results demonstrate a weakly positive relationship between PTG and PTSS, which only achieves statistical significance because of the very large sample size.

The presented study is the largest to date examining the relationship of PTSS to PTG. However, some study limitations must be considered. Small adaptations were made to the PTSS and PTG measures, and all survivors were at least 15 years since their diagnosis of cancer. Furthermore, greater than one third of the sample was below the age of 5 years at the time of their cancer diagnosis. These factors may have attenuated the traumatic impact, and appreciation of the life-threatening nature of the illness, thus contributing to the relatively weak association observed between PTS and PTG. However, there was also ample time for late effects of cancer treatment to emerge. Nevertheless, substantial levels of PTSS and growth were reported, with scores across the entire range of both study instruments, and with this large, geographically and demographically diverse sample, a weak, positive relationship between PTS and PTG is evident.

The current findings may help to explain some of the inconsistent findings reported in the literature. If the true relationship between PTG and PTSS in the cancer survivor population is weakly positive, smaller sample studies that vary around this are likely to vary between near zero and moderately positive. From a theoretical perspective, despite the statistical significance, these current data suggest that PTS and PTG might best be considered as largely independent constructs. Certainly one cannot conclude that significant PTSS must be present for growth to occur. Scores across the entire range of the PTGI were observed in the absence of any PTSS (data not shown). Thus, we conclude that theories suggesting that posttraumatic stress is prerequisite for PTG should be reconsidered.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1

Factors Associated with Posttraumatic Growth (Partial Proportional Odds Model): Factors Meeting Proportional Odds Assumption

Covariate	Odds Ratio	95% CI	p-value
Sex			
(Female vs. Male)	1.46	(1.32– 1.61)	<0.0001
Education Level			
(>High School vs. <=High School)	0.88	(0.76– 1.02)	0.09
(Post Graduate vs. <=High School)	0.90	(0.74– 1.09)	0.27
Ever Been Employed			
(Yes vs. No)	1.00	(0.87– 1.13)	0.95
Marital Status			
(Married/Living as Married vs. Single)	1.08	(0.88– 1.33)	0.44
(Divorced/Separated/Widow vs. Single)	1.13	(1.00– 1.27)	0.04
Ethnicity			
(Other vs. non-Hispanic White)	1.23	(1.06– 1.43)	<0.01
Years since Diagnosis			
(20–24 vs. 15–19)	0.92	(0.82– 1.05)	0.21
(25–29 vs. 15–19)	0.91	(0.80– 1.05)	0.21
(30–34 vs. 15–19)	0.86	(0.72– 1.03)	0.11
Subsequent Malignant Neoplasm(SMN) or recurrence			
(Yes vs. No)	1.62	(1.42– 1.85)	<0.0001
Chemotherapy			
(Anthracyclines/Alkylators vs. None)	1.70	(1.50– 1.93)	<0.0001
(Other Drugs vs. None)	1.28	(1.09– 1.51)	<0.01
Brain Radiation Therapy(RT)			
(RT not to site vs. No RT)	1.01	(0.90– 1.14)	0.83
(RT to site or Total Body Irradiation vs. No RT)	1.12	(0.99– 1.26)	0.08
(RT, Unknown site vs. No RT)	1.50	(1.10– 2.05)	<0.01

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Factors not Meeting Proportional Odds Assumptions

	≥4th Quartile			≥3rd Quartile			≥2nd Quartile		
	Odds Ratio	**95 % CI**	**p-value**	**Odds Ratio**	**95 % CI**	**p-value**	**Odds Ratio**	**95 % CI**	**p-value**
Personal Income									
($20K–$39,999 vs <$20K)	1.08	(0.92– 1.26)	0.34	1.13	(0.98– 1.30)	0.10	1.11	(0.95– 1.30)	0.19
($40K > vs <$20K)	0.79	(0.66– 0.94)	<0.01	0.96	(0.82– 1.12)	0.60	1.18	(0.99– 1.41)	0.06
PTSS (Quartile)									
2nd vs 1st	1.12	(0.94– 1.33)	0.21	1.35	(1.17– 1.57)	<0.0001	1.51	(1.29– 1.77)	<0.0001
3rd vs 1st	1.10	(0.92– 1.32)	0.30	1.50	(1.28– 1.75)	<0.0001	2.03	(1.70– 2.42)	<0.0001
4th vs 1st	1.07	(0.90– 1.29)	0.43	1.30	(1.12– 1.52)	<0.001	2.16	(1.80– 2.58)	<0.0001
Age at Diagnosis (years)									
(5–9 vs 0–4)	1.1	(0.93– 1.31)	0.27	1.22	(1.05– 1.42)	<0.01	1.37	(1.16– 1.62)	<0.001
(10–14 vs 0–4)	1.31	(1.09– 1.57)	<0.01	1.49	(1.27– 1.74)	<0.0001	1.63	(1.35– 1.96)	<0.0001
(15–20 vs 0–4)	1.29	(1.06– 1.56)	0.01	1.60	(1.35– 1.91)	<0.0001	2.13	(1.74– 2.62)	<0.0001

Note. CI = confidence interval; PTSS = posttraumatic stress symptoms; PTSS Quartile 1 = PSDS Total Score of 0; PTSS Quartile 2 = PSDS Total Score of 1–3; PTSS Quartile 3 = PSDS Total Score of 4–8; PTSS Quartile 4 = PSDS Total Score of 9–51. PTG Quartile 1 = PTGI Total Score of 0–33; PTG Quartile 2 = PTGI Total Score of 34–58; PTG Quartile 3 = PTGI Total Score of 59–75; PTG Quartile 4 = PTGI Total Score of 76–105.