Published in final edited form as:

Psychooncology. 2013 August ; 22(8): 1774–1782. doi:10.1002/pon.3213.

Parenting Stress and Neurocognitive Late Effects in Childhood Cancer Survivors

Sunita K. Patel, Ph.D.¹, Andrew Wong, MA^{1,2}, Michelle Cuevas, Ph.D.^{1,3}, and Hillary Van Horn, Ph.D.¹

¹Departments of Population Sciences, Pediatrics, and Supportive Care Medicine, City of Hope Medical Center & Beckman Research Institute, Duarte, California

²Fuller Theological Seminary, Pasadena, CA

³California School of Professional Psychology at Alliant International University, Los Angeles, CA

Abstract

Objective—Surveillance of neurocognitive late effects has typically focused on the pediatric survivor alone and rarely has focused on the potential family burden. We investigated the impact of child neurocognitive effects on parenting stress, and hypothesized that parents of childhood cancer survivors with greater executive difficulties experience higher stress relative to parents of children with less adverse impact.

Method—Parents of 44 children who survived cancer involving CNS-directed treatments and who had documented neurocognitive deficits completed standardized questionnaires assessing their perceived level of stress and perception of their child's executive functioning abilities in daily life. Data from performance-based cognitive tests were obtained on the children. Multivariate regression models examined socio-demographic, clinical, and child's executive functioning as predictors of parent stress. Differences in parenting stress based on child's level of executive functioning were evaluated.

Results—Parent stress was significantly associated with both performance-based and parent report measures of child executive functioning. Child executive functioning significantly predicted parent stress even after controlling for socio-demographic and clinical factors, and the final model accounted for 42% of variance in parent stress levels. Significant differences in parent stress were found when comparing higher versus lower levels of child executive functioning. The nature of the executive difficulties, however, appears important, as we found increased parenting stress among children with behavioral regulation problems rather than metacognitive difficulties.

Conclusions—The associations between parenting stress and neurocognitive problems found in this study suggests the need for further research, along with professional monitoring and appropriate intervention.

Keywords

childhood cancer; neurocognitive; parent; stress; survivor; pediatric cancer

Neurocognitive late effects following pediatric cancer and/or its treatment have been extensively documented over the past two decades. Adverse impact on specific areas of cognition have been linked to treatments such as cranial radiation and high-dose

chemotherapies such as methotrexate.[1–3] Research consistently demonstrates treatment-related deficits in core neurocognitive processes such as attention, executive functioning, and processing speed in subgroups of at risk survivors.[1–3] These deficits interfere with age-appropriate acquisition of knowledge so that overtime declines may emerge in IQ and academic achievement scores.[4,5] Additionally, impairments in social and behavioral functioning are also associated with learning and neurocognitive late effects.[6–8]

While late effects continue to garner increased attention in the literature, there is little focus on how the child's functional status as a survivor impacts the larger family system, including parents and/or caregivers. Much of the focus to date has revolved around generalized parental stress during the course of a child's cancer diagnosis and treatment.[9] In such research it is noted that the strain related to changes in roles and responsibilities during the care of a critically ill child is pervasive, affecting employment, finances, social support, marital relations, self-care, personal health and the family structure itself.[10] While the active treatment itself does end, some of these stressors may not remit following completion of treatment. The majority of parents experience a return to normal mental health; however, some parents report prolonged stress even years after initial cancer diagnosis.[11,12] Persistent parental stress in the months following completion of the child's cancer treatments has been associated with severity of anxiety experienced close to the diagnosis stage [13], but reasonably may also be related to the new problems and challenges associated with the child's reintegration into an age appropriate environment. Emergence of neurocognitive late effects, delays in emotional and social competence, prolonged parental dependence, and increased need for parent advocacy efforts with educational systems [14] are only some problems that parents of children with potentially neurotoxic therapy may face years after treatment.

One study of mothers of childhood cancer survivors found that maternal stressors and worries were largely related to fears of cancer recurrence, after effects of treatment, and concerns of psychosocial difficulties in their child. [15] Notably, mothers of children with more severe limitations expressed greater concerns. Cognitive deficits in particular were related to increased levels of worry regarding their child's potential to be well-adjusted and happy. The presence of such deficits would understandably cause concern in parents, as disabilities may limit the child's capacity for independent functioning as an adult. Aside from such concerns about their child's future status, we speculated that neurocognitive late effects may trigger parental stress in a more "here-and-now" daily basis due to the child's need for increased parental supervision and support. Specifically, children with impairments in attention and executive functioning skills typically require greater assistance with planning and preparing for tasks that other children manage independently. In Abidin's widely recognized model of parenting stress, demanding characteristics in children increase parents' stress.[16] Among some pediatric populations, child characteristics associated with neurocognitive disability, particularly executive deficits appear to cause stress as these challenges are often manifested behaviorally in daily life.[17–19] Associations between parenting stress and level of impairment has been observed in children with Asperger's syndrome where executive functioning is impaired despite adequate intellectual functioning. [19] Research on the family impact of children with learning disabilities, including ADHD, show higher parental or caregiver stress particularly when the child has impaired emotional regulation and exhibits overt behavioral problems.[20–22] In their study of the association between parenting stress and cognitive functioning in children with Fetal Alcohol Spectrum Disorders, Paley et al. reported that rather than general cognitive impairment (i.e. IQ), the child's difficulties in planning, organizing and self-regulating their behavior in everyday life was especially stressful to parents.[16]

While it seems reasonable to speculate that parents of childhood cancer survivors are at increased risk for stress if their child has neurocognitive dysfunction, particularly in executive functioning, this has not been investigated. Understanding the relevance of the child's cognitive functional status to caregiver stress has applicability for clinical practice as high parent stress is associated with suboptimal parenting practices and lower overall family functioning. [23 –24] We report on an investigation using data from a larger study to examine our hypothesis that child executive dysfunction in cancer survivors contributes towards parenting stress. In particular, we speculated that parents of childhood cancer survivors with greater executive difficulties may experience higher stress relative to parents of children with less adverse impact.

Executive function is a general construct that includes all supervisory or self-regulatory functions which organize and direct cognitive activity, emotional response, and overt behavior.[25] Measurement of executive function is complex and it is increasingly accepted that traditional, performance-based cognitive tests may not provide a sufficient assessment of the integrated executive system or real world functioning.[40] Specifically, performance-based measures tend to sample discrete aspects of executive function over a short period in the highly structured and interactive testing setting. In the testing situation, the examiner serves as the child's external executive and so children can perform adequately in spite of executive impairments.[41] While also not without any limitations, parent or teacher report is viewed as a relatively more ecologically valid assessment of the child's executive functioning in the everyday environment.[40] With this background in mind, a validated and reliable parent report measure was used as the primary measure of the child's executive functioning to evaluate impact on parent stress. However, we also included performance-based cognitive tests as a secondary measure of executive functioning with the understanding that both approaches may tap separable functions. [42]

Method

Procedures

The sample was recruited from the Pediatrics Department at City of Hope Cancer Center for this IRB approved study. Forty-four parents of children who had survived cancer involving CNS-directed treatments and who had documented neurocognitive deficits were administered standardized questionnaires assessing their perceived level of stress and perception of their child's executive functioning abilities. The parents had responded to an invitation letter and/or brochure in the clinic recruiting for a pilot behavioral/educational intervention study for parents of children with cancer-related neurocognitive and adaptive difficulties. The questionnaires were completed by parents of eligible survivors as part of the baseline packet of measures prior to randomization for the pilot intervention study.

Families were eligible if the child was in remission and 6 months post treatment, the child was between the ages of 6 and 18 and did not have a severe psychiatric or neurological disorder, the child had evidence of existing cognitive and adaptive difficulties on neurocognitive assessment, which was part of the eligibility screening procedure for the larger study, and both the primary parent participant and child were English speaking. (Parents could be bilingual but had to have adequate English fluency). An exclusion criterion was history of brain tumor diagnosis in the child since the larger study was an intervention study for children with mild to moderate neurocognitive dysfunction, rather than for the more severe deficits frequently observed in survivors of malignant brain tumors. In addition to brochures in the clinic waiting room, recruitment for the larger study consisted of invitation letters mailed to one hundred eight families who were identified from institutional databases as meeting initial eligibility criteria. Among the 108, the age for 20 children exceeded the eligibility criteria by the time updated contact information was

obtained and staff made verbal phone contact. From the remaining 88, 20 (23%) were excluded following phone contact due to parental report of good cognitive and academic functioning in their child; an additional 8% (n=7) were excluded due to premorbid or comorbid difficulties including severe psychiatric disorder and pervasive developmental diagnosis. From the remaining 61 eligible families, 43(71%) consented to the pilot study. Reason for study decline (29%) typically was distance and/or lack of time. One additional out-of-state eligible family requested to join the study and was also enrolled (N = 44).

Participants

Forty-four primary participating parents enrolled in the study, 86% of whom were mothers. The majority of the sample was White, including Hispanic Americans (57%) and Anglo Americans (23%), and was married (70%). The majority of parents were employed, with 39% full-time employed and 27% part-time. 7% were attending school, and 27% were homemakers and/or unemployed, or on temporary leave. Additional parent demographics are presented in Table 1. The average age of the children at study entry was 11.92 years. The average age of the child at initial cancer diagnosis was 4.91 years. Thirty seven of the 44 children (84%) in the study had a history of leukemia diagnosis, four had Non-Hodgkin's lymphoma, and three had other non-brain tumor cancer diagnoses resulting in hematopoietic stem cell transplantation (Table 1).

Measures

Executive functioning—The Behavior Rating Inventory of Executive Function (BRIEF) parent report questionnaire was used to assess child executive functioning late effects.[25] The BRIEF consists of 86 items which assess the child's behavior in daily life on a 3-point Likert scale and scores are obtained to assess eight aspects of the executive functioning construct, including: (a) working memory, (b) inhibitory control, (c) ability to shift attention and cognitive resources, (d) modulate emotional responses, (e) initiate activities, (f) plan and organize, (g) evaluate their own functioning, and (h) organize materials. These subscales are then organized into two separate indices, the Behavioral Regulation Index [BRI] (child's ability to inhibit and modulate emotions and behavior) and the Metacognition Index (MCI) (child's ability to initiate, plan, organize, and sustain problem-solving in working memory), and one overall score, the Global Executive Composite, which incorporates all eight subscales. The normative sample for the BRIEF was comprised of 1419 parents. Cronbach's α ranged from .80 to .98, with good convergent and discriminant validity.

Performance-based cognitive measures—As previously indicated, all children underwent a neurocognitive screen to confirm the presence of neurocognitive late effects as part of the eligibility criteria for the larger intervention study. Selected performance-based cognitive tests were used to evaluate the research objectives of this study. In particular, we focused on tests of selected executive functions (attention and working memory skills) as assessed by the Wechsler Intelligence Scale for Children – 4th Edition (WISC-IV) [26] subtests.

The WISC-IV is a widely used instrument to assess global intellectual functioning in individuals 6–16 years of age. The adult version, the WAIS-IV, is used for children older than 16 years. It is comprised of several subtests each measuring specific cognitive abilities, with estimated internal consistency reliability coefficients ranging from 0.81 to 0.97. Construct validity, criterion validity, and test-retest reliability have been well established. The WISC-IV *Working Memory Index* (WMI) is comprised of scores on the *Digit Span* and the *Letter-Number Sequencing* subtests designed to measure working memory skills. The term “working memory” generally describes an aspect of executive functioning, and refers to the capacity to direct and control one's resources sufficiently to hold information briefly

in mind while performing some action or cognitive operation on it. The *Digit Span* test is composed of two parts, in the first part the child is required to repeat strings of digits of increasing length, and in the second part the digits have to be repeated backwards. The first part, *Digit Span Forwards*, predominantly measures attention, while the second part *Digit Span Backwards*, is a more effortful activity that is regarded as the prototype test of working memory as it requires the child to mentally hold information “on line” while performing cognitive manipulations.

The WISC-IV *Processing Speed Index* is comprised of the WISC-IV *Coding* and *Symbol Search* subtests, both paper and paper tasks in which the child has to process and respond to visual stimuli rapidly, with processing speed as the primary cognitive function being assessed.[26] This index was included only in the exploratory analyses and to understand if any associations between WISC-IV Working Memory and parent stress would also be present on a performance-based measure that was primarily identified as testing a cognitive domain (i.e. processing speed) other than executive function.

Parenting stress—The 36 item Parenting Stress Index- Short Form (PSI/SF) [16] was used to measure parenting stress. On this standardized self-report questionnaire, parents respond to statements on a 5-point Likert scale (strongly agree to strongly disagree). The questionnaire consists of three subscales: (a) Parental Distress; (b) Parent-Child Dysfunctional Interaction and (c) Difficult Child, which can also be summed to obtain an overall score “*Total Stress*”. Similar to other research using the PSI/SF, raw scores were used for analyses. [27–28] Cronbach’s α ranged from .78 to .90.

Demographic questionnaire—Parents completed a demographic survey which also included a checklist of ten common stressors for parents to endorse if relevant: financial problems, recent family death, transportation problems, marital problems, legal problems, involvement with child protective services, child custody problems, health care or insurance problems, disability or psychiatric problem, employment problems, and an option for “other”. Those who did endorse stressors indicated that financial problems were one of the main issues (39%), 11% endorsed transportation problems, 7% marital problems, 7% legal problems, 7% health care or insurance problems, 9% disability or psychiatric problems, 16% problems with employment, and 9% endorsed “other” family stressor.

Medical and clinical information—Medical records were reviewed and cancer treatment for each child was assigned to one of four operationally defined categories of pediatric oncology treatment intensity using the Intensity of Treatment Rating scale–Second Edition (ITR-2): Least Intensive Treatment (Level 1), Moderately Intensive Treatment (Level 2), Very Intensive Treatment (Level 3), to Most Intensive Treatment (Level 4).[29] The ITR-2 has significant agreement between criterion ratings ($r = .95$) and has high inter-rater reliability ($r = .87$).

Overview of statistical analyses—All analyses were conducted using SPSS (Statistical Package for the Social Sciences) version 19. From the sample of 44 parents and children, one BRIEF was only partially completed and so was not included in some analyses due to missing scores ($N=43$). Associations between child’s executive functioning and parent stress variables were examined using Pearson’s correlational analyses.

Given that parents typically experience stress for multiple reasons, some of which are not related to parenting, we evaluated the relative contribution of child executive functioning after controlling for selected socio-demographic and clinical factors in a hierarchical linear regression analyses with parenting stress as the criterion variable. Socio-demographic variables were entered as the first step and included child gender, father’s level of education,

and total number of family stressors (described in the methods section) endorsed by parent. Since the total sample size was relatively small and in keeping with the recommended minimum ratio of 5 cases for each predictor [43], we attempted to minimize the number of predictors entered in the model and selected demographic factors for step 1 based mostly on their significant relationship with parenting stress scores in simple regression univariate analyses. Specifically, father education rather than mother education was included in the multivariate regression model because only the former was significantly associated with PSI Total Stress score (Mother's Education: $r(44) = -.22, p = .15$; Father's Education: $r(44) = -.31, p = .04$). Child's gender but not child's age was entered into the model for the same reason (Child Age: $r(44) = .05, p = .76$; Child Gender: $r(44) = .27, p = .08$).

Clinical factors such as child's age at cancer diagnosis and the cancer treatment intensity rating were entered as the second step of the model. Measures of child executive functioning were entered in the third step.

Additional analyses included analysis of variance (ANOVA) to assess group differences in parent stress based on level of child's executive dysfunction as measured by the parent report BRIEF. The degree of power using a sample size of 43 to detect a difference between PSI Total Stress scores of one half standard deviation (.5 SD) at alpha level p less than .05 was estimated to be .80. Power to detect an observed R^2 of 0.30 in a fixed model linear multiple regression analyses with 8 predictors in a sample size of 45 at alpha level p less than .05 was estimated to be 80 percent.

Correlations to examine the associations between parent-report and performance-based indicators of child executive functioning were also conducted. Further detail regarding the statistical approach is integrated in the presentation of results below.

Results

Parent Stress and Child Executive Functioning as Measured by the BRIEF

Table 2a presents correlation coefficients between child's executive functioning, as measured by the BRIEF indices and subscales, and parent stress as measured by the PSI Total Stress score. Significant positive correlations of medium size emerged with the BRIEF BRI ($p < .01$), but not on the MCI, such that the higher the BRI score, the higher the parent stress score (higher scores connote greater executive difficulties and parent stress). All three of the BRI subscales (Inhibit, Shift, and Emotional Control) were correlated with parent stress. The majority of the group BRIEF mean scores were considerably less than reported for children with ADHD [44], but similar to the means for a group of children with moderate traumatic brain [40]. In our sample, the group mean scores were generally within the 50th and 75th percentile relative to normative means

Parent Stress and Child Executive Functioning as Measured by Performance-Based Measures

Table 2b presents correlation coefficients between child performance based measure of executive functioning (i.e. WISC-IV WMI and the individual subscales) and PSI Total Stress scores. A significant correlation of small to medium size was found with the WISC-IV WMI such that the lower the child's performance, the higher the parent stress ($p < .05$). The significant correlations were with Digit Span total and Digit Span backwards, rather than with the other subscales tapping other aspects of executive functions. Mean scores on the performance tests were mostly in the low average to average range, with the WISC-IV WMI score ($M = 85.36$) placing at the 16th percentile relative to population norms (lower scores connote greater difficulties). To explore if the association would be present on a cognitive performance task that mostly measured a function other than executive

functioning, we examined the correlation between PSI Total Stress score and the only other WISC-IV index available from the larger study, the Processing Speed Index. The processing speed index was not significantly correlated with parent stress, suggesting a possible specific association between executive functioning and parent stress.

Contribution of Child Executive Functioning Toward Parent Stress Relative to Demographic and Clinical Predictors

Given the finding of significant association between parent stress and both parent-report and performance-based measures of child executive functioning, the BRIEF indices and the WISC IV WMI was both included in the hierarchical regression model to evaluate the relative contribution of child executive functioning after controlling for socio-demographic and clinical factors.

Step 1 was significant, $R^2(3, 39) = 0.22, p = .02$, with socio-demographic factors explaining 22% of the variance in parent stress (Table 3). The change in R^2 was not significant for Step 2, but was for Step 3, $R^2(3, 34) = 0.42, p = .03$, with child's executive functioning explaining an additional 17% of parenting stress above demographic and clinical factors. The final model accounted for 42% of variance in parenting stress levels ($R^2 = .42, F(8, 34) = 3.37, p = .03$). The beta weights and significance values, presented in Table 3, indicates which variables contributes most to predicting parent stress. With this combination of predictors, the BRIEF BRI has the highest beta (.39), and is the only child executive functioning variable that contributed significantly.

Differences in Parent Stress Based on Lower Versus Higher Scores on BRIEF

Given the findings of a significant contribution towards the variance in parenting stress, we explored differences in parenting stress based on the level of child executive functioning, as measured by the BRIEF. The sample was categorized into two groups based on the T-score of the parent BRIEF, with the "higher" group defined as placing at least one standard deviation above the normative mean (T score >60), and the remaining placing within the "lower" group. The BRIEF manual defines clinically significant levels as $T > 65$, or approximately at or exceeding 90th percentile; however, this criteria is viewed as highly conservative and also most commonly demonstrated in children with ADHD. The relative probability of obtaining a clinically elevated score using the conservative criteria varies depending on diagnostic groups and a number of studies have used a T-score of 60 or above to allow for the inclusion of "mildly elevated scores" (t-scores equaling between 60–64 [45]). [46–47] Unlike childhood cancer survivors of brain tumor, leukemia survivors are typically expected to demonstrate difficulties that are relatively mild to moderate rather than severe [2], and a T-score cut > 60 was deemed reasonable to evaluate for this preliminary investigation in a sample of mostly leukemia survivors with documented neurocognitive late effects.

One-way ANOVAs were conducted to compare the two groups using the index and sub-index scores of the BRIEF as the independent variable, and the PSI Total Stress scores as the dependent variable (i.e. higher versus normal child executive functioning to predict parenting stress). Relevant statistics means, and standard deviations are displayed in Table 4. Given that we conducted the ANOVA on all the BRIEF composite scales and subscales, each ANOVA was tested at the .005 level after applying the Bonferroni approach to control for Type I error ($.05/10 = .005$). Results showed a significant difference in parenting stress when comparing the two groups on the BRIEF BRI score (Table 4). The mean Total Stress score for the group of children with lower executive dysfunction placed at the 50th percentile (within normal range) using the PSI reference norms, while the mean Total Stress score for

the group with higher child executive dysfunction placed at the 90th percentile, a clinically significant level of stress.

No significant differences in parenting stress emerged when examining the MCI Index. Differences approached significance for two of the three subtests that comprise the BRI Score, the BRIEF Inhibit and Shift subtests, at the $p = .03$ level. The ANOVA results suggest that the child's degree of executive functioning difficulties, manifested in more behavioral dimensions, likely are related to parenting stress.

Associations between Parent and Performance-Based Measures of Child Executive Functioning

Correlations significant at $p < .05$ between BRIEF subscale T-scores and the WISC-IV WMI and subtests are presented in Table 5. No correlations were significant at $p < .01$ (Table 5). Specifically, the WISC-IV WMI and the BRIEF working memory subscale were significantly correlated, as expected from a theoretical perspective given the greater cognitive load relative to behavioral load typically connected with the concept of "working memory". However, the overall Digit Span subtest, as well as Digit Span Backwards, were also significantly correlated with BRIEF subscales from the BRI index, typically viewed as tapping more behavioral regulation dimensions. Given the modest correlations and possibility of type 1 error, it is difficult to interpret these associations. It is also true that this overall lack of consistent concordance between the behavioral (i.e. parent observations, etc) measures and the performance-based cognitive tests of executive functioning has been previously reported [42, 48], and may reflect shared but also unique differences in the cognitive and behavioral processes tapped by the different assessment approaches.

Discussion

Findings support our hypothesis that parents of childhood cancer survivors with neurocognitive late effects, particularly with executive functioning difficulties, are at risk for caregiver stress and warrant monitoring for assistance. Surveillance of neurocognitive late effects has typically focused on the pediatric survivor alone, including long-term outcomes related to independence and social competence as young adults, but rarely has focused on the potential family burden.

Results from our analyses found that parenting stress was significantly associated with both performance-based and parent report measures of child executive functioning. In multivariate regression analyses, child executive functioning significantly predicted parenting stress even after controlling for socio-demographic and clinical factors. Analyses of variance results indicated differences in parent stress based on the level of child impairment, with significantly higher stress among parents of survivors with relatively more executive difficulties.

The nature of the executive difficulties, however, appears important, as we found increased parenting stress among children with difficulties in the behavioral regulation domain rather than in the metacognitive domain. Additionally, in our regression model which included predictors from both parent and performance-based measures of child executive functioning, the BRIEF BRI was the only measure that significantly contributed toward the variance in parenting stress. Essentially, child weaknesses in the working memory capacity, as measured by the WISC-IV, or as measured by the BRIEF MCI, were not as robustly associated with parenting stress as were difficulties which are less exclusive to cognitive control (i.e. regulatory control of emotional response and behavioral action, etc.). This finding is akin to the ADHD literature where behavioral difficulties in the child, including problems in inhibition, are noted to require greater parental management and are more

disruptive to the family environment.[33] Based on a study of 144 families 1 to 12 years post-cancer treatment, poor behavioral control and high anxiety among childhood cancer survivors was speculated to lead to poorer communication patterns, poorer role distributions, and difficulties with affective involvement within a family system.[34]

Differences in the parent report versus performance-based assessment approach of child executive functioning warrants some consideration in interpreting the findings. While the WISC-IV Working Memory Index was significantly correlated with the BRIEF working memory scale in our sample as expected, the overall pattern of WISC-IV associations with the two different indices of the BRIEF was not consistent. We speculate that there probably exists both shared and unique variance among the different assessment approaches. Another consideration is that the performance-based tests of executive functioning used in this study were limited to the WISC-IV, and also represented mostly attention and working memory processes, rather than multiple aspects of executive functioning such as inhibition, cognitive flexibility, and maintaining set, etc.

In general, results from the various analyses conducted in this study do provide preliminary data supporting a relationship between child neurocognitive functioning and parenting stress, and points to the need for future research in this area. Our very exploratory look at the association between WISC-IV Processing Speed Index and parenting stress suggests that it might be important to determine whether specific neurocognitive late effects, such as executive functioning, pose more stress relative to impairments in other cognitive domains.

Some degree of a bidirectional relationship between parenting stress and the child's neurobehavioral functioning also warrants consideration in future research, and has been advocated as a conceptual framework to understand family impact of neurocognitive late effects.[35] Specifically, while neurocognitive and behavioral late effects may result in parenting stress and increase family burden, family factors likely also influence the children's adjustment to late effects.[35] Family stress has been reported as a predictor of maladaptive behavior in survivors of pediatric brain tumor.[36]

A limitation of this study is that it is a cross-sectional examination at a time when neurocognitive effects had already emerged, rather than a prospective, longitudinal examination of changes in parenting stress or family impact as the late effects emerged. Another limitation is that this sample does not represent the full range of parents with leukemia survivors who have neurocognitive difficulties; rather it is a potentially biased group of parents who responded to an invitation to learn ways they could help their child improve their learning and school success. In other words, these were a group of motivated parents who were involved in their child's lives.

In summary, our results suggest that the nature and extent of the child's neurocognitive problems likely play a contributory role toward parenting stress and follow-up intervention may be beneficial for optimal family functioning. Our previous work suggests parental distress may be underestimated by psychosocial staff even in the active cancer treatment phase, and should be actively assessed, along with the child's adjustment. [37] In addition to interventions to improve coping, it is important to increase the parent's understanding of the child's specific neurocognitive deficits and ways it impacts daily tasks. Hassall et al. found that among their sample of 46 mothers of children with intellectual disabilities, mothers with lower understanding of their child's condition and lower knowledge of ways to support their child experienced significantly more stress compared to the mothers with higher understanding and knowledge.[21] In extrapolation, parents of childhood cancer survivors with neurocognitive late effects likely would benefit from education and guidance on how best to manage their child's neurobehavioral issues and unique needs, and at the least to

understand impact in daily life. Treatment of parent distress may also result in reduced behavioral and emotional problems in children. [38]

Acknowledgments

Funding:

NIH NCI RO3 CA130731 (S. Patel)

References

1. Spiegler BJ, Bouffet E, Greenberg ML, Rutka JT, Mabbott DJ. Change in neurocognitive functioning after treatment with cranial radiation in childhood. *Journal of Clinical Oncology*. 2004; 22(4):706–713. [PubMed: 14966095]
2. Nathan PC, Patel SK, Dilley K, et al. Guidelines for identification of, advocacy for, intervention in neurocognitive problems in survivors of childhood cancer: a report from the Children's Oncology Group. *Archives of Pediatric & Adolescent Medicine*. 2007; 161:798–806.
3. Moleski M. Neuropsychological, neuroanatomical, and neurophysiological consequences of CNS chemotherapy for acute lymphoblastic leukemia. *Archives of Clinical Neuropsychology*. 2000; 15(7):603–630. [PubMed: 14590198]
4. Palmer SL, Golubeva O, Reddick WE, et al. Patterns of intellectual development among survivors of pediatric medulloblastoma: A longitudinal analysis. *Journal of Clinical Oncology*. 2001; 19(8): 2302–2308. [PubMed: 11304784]
5. Mabbott DJ, Spiegler BJ, Greenberg ML, Rutka JT, Hyder DJ, Bouffet E. Serial evaluation of academic and behavioral outcome after treatment with cranial radiation in childhood. *Journal of Clinical Oncology*. 2005; 23(10):2256–2263. [PubMed: 15800316]
6. Aarsen FK, Paquier PF, Reddingius RE, et al. Functional outcome after low-grade astrocytoma treatment in childhood. *Cancer*. 2006; 106:396–402. [PubMed: 16353203]
7. Reimers TS, Mortensen EL, Nysom K, Schmiegelow K. Health-Related Quality of Life in Long-Term Survivors of Childhood Brain Tumors. *Pediatric Blood & Cancer*. 2009; 53:1086–1091. [PubMed: 19499581]
8. Vannatta K, Gerhardt CA, Wells RJ, Noll RB. Intensity of CNS treatment for pediatric cancer: Prediction of social outcomes in survivors. *Pediatric Blood and Cancer*. 2006; 49(5):716–722. [PubMed: 17096410]
9. Kazak AE, Boeving CA, Alderfer MA, Hwang WT, Reilly A. Posttraumatic stress symptoms during treatment in parents of children with cancer. *J Clin Oncol*. 2005; 23(30):7405–7410. (epub). [PubMed: 16157936]
10. Emond A, Eaton N. Supporting children with complex health care needs and their families: an overview of the research agenda. *Child: Care, Health and Development*. 2004; 30(3):195–199.
11. Streisand R, Braniecki S, Tercyak KP, Kazak AE. Childhood illness-related parenting stress: The pediatric inventory for parents. *Journal of Pediatric Psychology*. 2001; 26(3):155–162. [PubMed: 11259517]
12. Hoekstra-Weebers JE, Jaspers JP, Kamps WA, et al. Psychological adaptation and social support of parents of pediatric cancer patients: a prospective longitudinal study. *J Pediatr Psychol*. 2001; 26:225–235. [PubMed: 11329482]
13. Kazak AE, Barakat LP. Brief report: Parenting stress and quality of life during treatment for childhood leukemia predicts child and parent adjustment after treatment ends. *Journal of Pediatric Psychology*. 1997; 22(5):749–758. [PubMed: 9383934]
14. Radcliffe J, Bennett D, Kazak AE, Foley B, Philips P. Adjustment in childhood brain tumor survival: Child, mother, and teacher. *Journal of Pediatric Psychology*. 1996; 21:529–539.
15. Zebrack B, Chesler M, Orbuch TL, Parry C. Mothers of survivors of childhood cancer. *Journal of Psychosocial Oncology*. 2002; 20(2):1–25.
16. Abidin, R. Parenting Stress Index (3rd Ed.): Professional Manual PSI-3 Short Form. Odessa, FL: Psychological Assessment Resources, Inc.; 1995.

17. Paley B, O'Connor MJ, Frankel F, Marquardt R. Predictors of stress in parents of children with fetal alcohol spectrum disorders. *Journal of Developmental and Behavioral Pediatrics*. 2006; 27(5):396–404. [PubMed: 17041276]
18. Graziano PA, McNamara JP, Geffken GR, Reid A. Severity of children's ADHD symptoms and parenting stress: a multiple mediation model of self-regulation. *J Abnorm Child Psychol*. 2011 Oct; 39(7):1073–1083. [PubMed: 21629991]
19. Epstein T, Saltzman-Benaiah J, O'Hare A, Goll JC, Tuck S. Associated features of Asperger Syndrome and their relationship to parenting stress. *Child Care Health Dev*. 2008 Jul; 34(4):503–511. [PubMed: 19154552]
20. Harrison C, Sofronoff K. ADHD and parental psychological distress: Role of demographics, child behavioral characteristics, and parental cognitions. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2002; 41(6):703–711. [PubMed: 12049445]
21. Hassall R, Rose J, McDonald J. Parenting stress in mothers of children with an intellectual disability: The effects of parental cognitions in relation to child characteristics and family support. *Journal of Intellectual Disability Research*. 2005; 49(6):405–418. [PubMed: 15882391]
22. Saloviita T, Itäläinen M, Leinonen E. Explaining the parental stress of fathers and mothers caring for a child with intellectual disability: A double ABCX model. *Journal of Intellectual Disability Research*. 2003; 47(4–5):300–312. [PubMed: 12787162]
23. Brody GH, Flor DL. Maternal psychological functioning, family processes, and child adjustment in rural, single-parent, African American families. *Developmental Psychology*. 1997; 33:1000–1011. [PubMed: 9383622]
24. Simons RL, Beaman J, Conger RD, Chao W. Stress, support, and antisocial behavior traits as determinants of emotional well-being and parenting practices among single mothers. *Journal of Marriage & the Family*. 1993; 55:385–398.
25. Gioia, G.; Isquith, P.; Guy, S.; Kenworthy, L. *The Behavior Rating Inventory of Executive Function (BRIEF): A Professional Manual*. Odessa, FL: Psychological Assessment Resources; 2000.
26. Wechsler, D. *Wechsler Intelligence Scale for Children (4th Edition)*. San Antonio, TX: The Psychological Corporation; 2003.
27. Baker DB. Parenting stress and ADHD: A comparison of mothers and fathers. *Journal of Emotional and Behavioral Disorders*. 1994; 2(1):46–50.
28. Quittner AL, Glueckauf RL, Jackson DN. Chronic parenting stress: Moderating versus mediating effects of social support. *Journal of Personality and Social Psychology*. 1990; 59(6):1266–1278. [PubMed: 2283593]
29. Werba BE, Hobbie W, Kazak AE, Ittenbach RF, Reilly AF, Meadows AT. Classifying the intensity of pediatric cancer treatment protocols: The Intensity of Treatment Rating scale 2.0 (ITR-2). *Pediatric Blood Cancer*. 2007; 48(7):673–677. [PubMed: 17427232]
30. Wechsler, D. *Wechsler Individual Achievement Test-II (2nd Edition)*. San Antonio, TX: The Psychological Corporation; 2001.
31. Delis, D.; Kramer, JH.; Kaplan, E.; Ober, BA. *The California Verbal Learning Test-Child Manual*. San Antonio, TX: The Psychological Corporation; 1994.
32. Cohen, M. *Children's Memory Scale*. San Antonio, TX: The Psychological Corporation; 1997.
33. Kashdan TB, Jacob RG, Pelham WE, et al. Depression and anxiety in parents of children with ADHD and varying levels of oppositional defiant behaviors: Modeling relationships with family functioning. *Journal of Clinical Child and Adolescent Psychology*. 2004; 33(1):169–181. [PubMed: 15028551]
34. Alderfer MA, Navsaria N, Kazak AE. Family functioning and posttraumatic stress disorder in adolescent survivors of childhood cancer. *Journal of Family Psychology*. 2009; 23:717–725. [PubMed: 19803607]
35. Peterson CC, Drotar D. Family impact of neurodevelopmental late effects in survivors of pediatric cancer: review of research, clinical evidence, and future directions. *Clin Child Psychol Psychiatry*. 2006; 11(3):349–366. [PubMed: 17080773]
36. Carlson-Green B, Morris RD, Krawiecki NS. Family and illness predictors of outcome in pediatric brain tumors. *Journal of Pediatric Psychology*. 1995; 20:769–784. [PubMed: 8558377]

37. Patel SK, Mullins W, Turk A, Dekel N, Kinjo C, Sato J. Distress screening, rater agreement, and services in pediatric oncology. *Psycho-oncology*. 2011 Dec; 20(12):1324–1233. [PubMed: 20925136]
38. Gunlicks ML, Weissman MM. Change in child psychopathology with improvement in parental depression: A systematic review. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2008; 47(4):379–389. [PubMed: 18388766]
39. Hollingshead, AB. Four Factor Index of Social Status. New Haven, CT: Yale University Press; 1975.
40. Gioia GA, Isquith PK, Kenworthy L, Barton RM. Profiles of everyday executive function in acquired and developmental disorders. *Child Neuropsychology*. 2002; 8:121–137. [PubMed: 12638065]
41. Silver CH. Ecological validity of neuropsychological assessment in childhood traumatic brain injury. *Journal of Head Trauma Rehabilitation*. 2000; 15:973–988. [PubMed: 10876170]
42. Anderson VA, Anderson P, Northam E, Jacobs R, Mikiewicz O. Relationships between cognitive and behavioral measures of executive function in children with brain disease. *Child Neuropsychology*. 2002; 8:231–240. [PubMed: 12759820]
43. Pedhazur, EJ. Multiple regression in behavioral research. Orlando, FL: Harcourt Brace; 1997.
44. Joyner KB, Silver CH, Stavinoha PL. Relationship between parenting stress and ratings of executive functioning in children with ADHD. *Journal of Psychoeducational Assessment*. 2009; 27:452–464.
45. Guy, SC.; Isquith, PK.; Gioia, GA. Behavior Rating Inventory of Executive Function—SR Manual. Lutz, FL: Psychological Assessment Resources; 1996.
46. Zabel TA, Jacobson LA, Zachik C, et al. Parent- and self-ratings of executive functions in adolescents and young adults with spina bifida. *The Clinical Neuropsychologist*. 2011; 25(6):926–941. [PubMed: 21955110]
47. Potter JL, Wade SL, Walz NC, et al. Parenting style is related to executive dysfunction after brain injury in children. *Rehabilitation Psychology*. 2011; 56(4):351–358. [PubMed: 21928918]

Table 1**Parent Demographic Information and Child Demographic and Clinical Information**

Variable	<i>n</i>	%
Parent information		
Age of primary parent at time of study (years) ^a	41.45 (9.66)	
Race/Ethnicity		
White (Hispanic/Latino is categorized as “White”)	35	80.00
Other	9	20.00
Predominant Language at home of primary caregiver		
English	39	88.60
Spanish	5	11.40
Primary parent’s education		
High school graduate or less	14	31.80
Some college (including business schools)	16	36.40
College graduate or postgraduate	14	31.80
Hollingshead Index of Social Position ³⁹		
Lower class	5	11.40
Lower-Middle class	11	25.00
Middle class	13	29.50
Upper-Middle class	12	27.30
Upper class	3	6.80
Child information		
Gender		
Male	21	47.70
Female	23	52.30
Age of child at time of study (months) ^a	143.07 (39.34)	
Age of diagnosis (months) ^a	58.93 (43.65)	
Type of diagnosis		
Acute Lymphocytic Leukemia (ALL)	31	70.50
Acute Myeloid Leukemia (AML)	6	13.60
Non-Hodgkin Lymphoma (NHL)	4	9.10
Other [treated with Bone Marrow Transplantation (BMT)]	3	6.80
Type of treatment		
Chemotherapy	43	97.70
Surgery	3	6.80
Cranial Radiation Treatment (CRT)	19	43.20
BMT/Hematopoietic stem cell transplantation (HSCT)	17	38.60
The Intensity of Treatment Rating Scale 2.0 (ITR-2)		
Least intensive	0	0.00
Moderately intensive	14	31.80

Variable	<i>n</i>	%
Very Intensive	9	20.50
Most Intensive	19	43.20

^aMean (*SD*)

Table 2Correlations of PSI Total Stress score with BRIEF index and subscale T-Scores ($N = 43$)

Variable	PSI Total Stress	BRIEF	
		<i>M</i>	<i>SD</i>
Parent BRIEF			
Behavioral Regulation Index	0.48 ^{**}	49.47	9.33
Inhibit	0.46 [*]	48.30	7.75
Shift	0.43 ^{**}	50.43	10.07
Emotional control	0.36 [*]	50.33	11.42
Metacognition Index	0.12	55.98	10.23
Initiate	0.17	53.60	10.49
Working memory	0.15	57.55	10.82
Plan/Organize	0.10	55.49	10.15
Organization of materials	−0.05	53.70	10.95
Monitor	0.15	53.86	10.33
PSI <i>M</i>	71.53		
PSI <i>SD</i>	21.99		

PSI, Parenting Stress Index; BRIEF, Behavior Rating Inventory of Executive Function.

*
 $p < 0.05$.**
 $p < 0.01$.

Table 3

Correlations of PSI Total Stress with WISC-IV measures ($N = 44$)

Variable	PSI Total Stress	WISC-IV	
		M	SD
WISC-IV			
Digit Span total scaled score	−0.36 [*]	7.44	2.92
Digit Span Forward scaled score	−0.24	7.45	2.65
Digit Span Backward scaled score	−0.36 [*]	8.35	2.97
Letter-Number Sequencing scaled score	−0.24	7.50	3.31
Working Memory Index	−0.32 [*]	85.36	15.11
Processing Speed Index	−0.10	91.44	13.41

Hierarchical Regression Analysis Predicting Total Parent Stress ($N = 43$)

Step and predictor variables	R^2	ΔR^2	<i>B</i>	<i>SE B</i>	95% CI	β	<i>t</i>	ΔF	<i>p</i>
Step 1:	.22							3.68	.02
Child's gender			8.86	6.09	[-3.52, 21.23]	.20	1.45		
Father's education			-3.98	1.92	[-7.88, -0.07]	-.30	-2.07*		
Total number of stressors endorsed			1.25	2.25	[-3.33, 5.83]	.08	0.56		
Step 2:	.24	.02						0.57	.57
Age at cancer diagnosis (months)			-0.02	0.08	[-0.18, 0.13]	-.05	-0.32		
ITR-2			4.54	3.60	[-2.78, 11.87]	.19	1.26		
Step 3:	.42	.17						3.37	.03
BRIEF Behavioral Regulation Index			20.90	7.96	[4.72, 37.07]	.39	2.63**		
BRIEF Metacognition Index			3.31	6.36	[-9.58, 16.26]	.07	0.53		
WISC-IV Working Memory Index			-0.22	0.20	[-0.62, 0.19]	-.15	-1.07		

PSI, Parenting Stress Index; WISC-IV, Wechsler Intelligence Scale for Children – Fourth Edition.

* $p < 0.05$.

** $p < 0.01$.

Note. ITR-2 = Intensity of Treatment Rating Scale 2.0; BRIEF = Behavior Rating Inventory of Executive Function; WISC-IV = Wechsler Intelligence Scale for Children – Fourth Edition.

*
 $p < .05$,
**
 $p < .01$.

Table 5

Means, standard deviations, and one-way analyses of variance for the BRIEF scales on the PSI Total Stress raw scores

Variable and Source	T score 60			T score > 60			MS	SS	F (1, 41)	p	η^2
	n	M	SD	n	M	SD					
BRIEF Indices											
Behavioral Regulation	34	66.50 ^a	20.74	9	90.56 ^b	15.80					
Between-group							2058.99	4117.98	10.42	0.002 *	0.20
Within-group							395.04	16196.72			
Inhibit	37	68.68	20.93	6	89.17	21.78					
Between-group							1083.88	2167.76	4.90	0.03	0.11
Within-group							442.61	18146.94			
Shift	33	67.64	23.23	10	84.40	9.96					
Between-group							1078.33	2156.66	4.87	0.03	0.11
Within-group							442.88	18158.04			
Emotional control	33	69.18	21.90	10	79.30	21.57					
Between-group							392.85	785.69	1.65	0.21	0.04
Within-group							476.32	19529.01			
Metacognition	27	68.63	24.17	16	76.44	17.35					
Between-group							306.23	612.46	1.28	0.27	0.03
Within-group							480.54	19702.23			
Initiate	32	68.50	22.26	11	80.36	19.49					
Between-group							576.08	1152.15	2.47	0.12	0.06
Within-group							467.38	19162.55			
Working memory	26	69.58	24.18	17	74.53	18.45					
Between-group							126.06	252.12	.52	0.48	0.01
Within-group							489.33	20062.58			
Plan/Organize	28	69.96	22.90	15	74.47	20.64					
Between-group							99.00	198.00	.40	0.53	0.01
Within-group							490.65	20116.70			
Organization of materials	28	71.25	25.21	15	72.07	14.98					
Between-group							3.26	6.51	.01	0.91	<0.01

Variable and Source	T score 60			T score > 60			MS	F (1, 41)	p	η^2
	n	M	SD	n	M	SD				
Within-group							20308.18	495.32		
Monitor	29	68.17	23.28	14	78.50	17.84				
Between-group							1007.06	503.53	2.14	0.15
Within-group							19307.64	470.92		0.05

* $p < 0.005$.

^a A score of this magnitude is at the 50th percentile, which represents normal levels of stress.

^b A score of this magnitude is at the 90th percentile, which represents clinically significant levels of stress.

Table 5
Correlations of BRIEF Subscale T-Scores with the WISC-IV Working Memory Index and Subtests

Measures ^a	BRIEF						
	Behavioral Regulation Index			Metacognition Index			
	Inhibit	Shift	EC	Initiate	WM	Plan/Organize	OoM Monitor
Working Memory Index	-.18	-.27	.10	-.12	-.29*	-.23	.06
Digit Span Total	-.30*	-.34*	.02	-.11	-.33*	-.19	.001
Digit Span Forward	-.18	-.27	-.06	-.18	-.29	-.30	-.30
Digit Span Backward	-.28	-.34*	.08	-.02	-.32*	-.06	-.01
Letter-Number Sequence	-.14	-.19	.14	-.14	-.21	-.26	.05

Note. (N=43); BRIEF=Behavior Rating Inventory of Executive Function; EC = Emotional Control; WM = Working Memory; OoM = Organization of Materials; WISC-IV = Wechsler Intelligence Scale for Children – Fourth Edition.

^aMeasures are in scaled or standard scores.

* p < .05.

** p < .01.