

literature hypothesizes that executive dysfunction contributes to suboptimal adaptive behavior outcomes in BT survivors; however, the aspects of EF that drive this relationship remain unexplored. Task-switching is an EF component that involves switching between concurrently presented tasks. This skill is critical for many day-to-day activities and may therefore contribute to observed adaptive functioning difficulties. This study investigates relationships between performance on two task-switching measures and adaptive behavior outcomes in BT survivors compared to healthy controls.

Participants and Methods: 86 survivors of pediatric BT ($M_{age}(SD) = 23.42(4.24)$, 44 females) and 86 age- and sex-matched controls ($M_{age}(SD) = 23.09(4.40)$, 44 females) from the Atlanta area completed the Delis-Kaplan Executive Function System Trail Making Test (TMT) and Verbal Fluency Test (VFT). Respectively, the Letter-Number Sequencing (LNS) and Category Switching (CS) conditions were isolated as measures of task-switching. Baseline conditions, representing the foundational skills needed to perform these timed task-switching measures rapidly (TMT: Letter Sequencing, Number Sequencing; VFT: Category Fluency), were included as covariates in all regressions. Informants familiar with the participants' daily living were interviewed with the Scales of Independent Behavior-Revised (SIB-R) to measure adaptive behavior in four domains (Motor Skills, Social Communication, Personal Living, Community Living). Linear regressions and t-tests confirmed group differences on task-switching performance and on adaptive functioning outcomes, respectively. Then, linear regressions investigated relationships between performance on each task-switching measure (LNS, CS) and SIB-R scores for survivors. A group by task-switching interaction was added to directly explore group differences in these relationships. $\alpha = .0125$ was used due to Bonferroni correction for the four SIB-R comparisons within each task-switching measure.

Results: BT survivors were more impaired than controls on LNS, CS, and SIB-R scores ($p < .05$, except Personal Living $p = .058$). For TMT, decreased performance on LNS predicted lower SIB-R scores in Social Communication ($p = .001$, $r^2_{semipartial} = .14$), Personal Living ($p = .002$, $r^2_{semipartial} = .13$), and Community Living ($p = .003$, $r^2_{semipartial} = .11$), but not Motor Skills ($p = .184$) in BT survivors. Strength of significant relationships was greater for survivors than

controls (all $p < .002$). For VFT, decreased performance on CS predicted lower SIB-R scores in Personal Living ($p = .036$, $r^2_{semipartial} = .06$) and Community Living ($p = .04$, $r^2_{semipartial} = .05$), but not in Motor Skills ($p = .716$) or Social Communication ($p = .14$) in BT survivors. Positive relationships between CS and SIB-R scores for all 4 domains were greater in survivors than controls ($p < .0125$).

Conclusions: These findings reveal a robust, positive relationship between task-switching performance and independent, daily behaviors that is specific to BT survivors. The relationship between LNS and Motor Skills may have been weakened by covariates involving baseline motor abilities; however, CS results suggest that task-switching is important for motor skills in survivors relative to controls. Community living skills were impaired in survivors and consistently related to task-switching performance. This work may inform interventions to target task-switching abilities and consequently, promote everyday living skills. Interventions aimed at vulnerabilities in adaptive behavior may help increase independence and quality-of-life as survivors transition to adulthood.

Categories: Cancer

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5 The Impact of Sex and Associations With Treatment Exposures on Neurocognitive Impairment in Pediatric Cancer Survivors: A report from the Childhood Cancer Survivor Study

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Objective: Sexual dimorphism in human brain structure and behavior is influenced by exposure to sex hormones during critical developmental periods. In children, cancer and cancer treatments may alter hormone activity and brain development, impacting neurocognitive functions.

Participants and Methods: Five-year survivors of childhood cancer (N=15,560) diagnosed at <21 years from 1970 to 1999, and 3,206 siblings from the Childhood Cancer Survivor Study completed the Neurocognitive Questionnaire (NCQ), a measure of self-reported task efficiency (TE), emotion regulation (ER), Organization, and working memory (WM). We compared rates of cognitive impairment (i.e., NCQ scores >90th percentile) in survivors and same-sex siblings, and sex differences in risk factors for cognitive impairment (i.e., treatment exposures, chronic health conditions (CHCs), cancer diagnosis, age at diagnosis) using modified Poisson regressions.

Results: Survivors were more likely to report cognitive impairment than same-sex siblings (Males: TE OR=2.3, p<.001; ER OR=1.7, p=.008; Organization OR=1.5, p=.04; WM OR=2.3, p<.001. Females: TE OR=2.6, p<.001; ER OR=1.9, p<.001; Organization OR=1.5, p=.02; WM OR=2.6, p<.001). Within survivors, females were more likely than males to report impairment in TE (OR=1.2, p=.001), ER (OR=1.5, p<.001), and WM (OR=1.2, p<.001). There were no sex differences in symptom severity in siblings (all ps>.05). Risk factors for cognitive impairment in survivors included cranial radiation dose (TE <20Gy OR=1.5, p=.008, ≥20Gy OR=2.5, p<.001; ER OR=1.5, p<.001; Organization <20 Gy OR=1.4, p<.001; < WM 20 Gy OR=1.8, p<.001, ≥20Gy OR=2.7, p<.001), presence of moderate to severe CHCs (TE 1 CHC OR=1.9, p<.001, >1 CHC OR=3.6, p<.001; ER 1 CHC OR=1.7, p<.001, >1 CHC OR=2.2, p<.001; Organization 1 CHC OR=1.5, p=.001, >1 CHC OR=2.5, p<.001; WM 1 CHC OR=1.8, p<.001, >1 CHC OR=4.1, p<.001). There were sex differences in cognitive impairment risk factors in survivors. In females, cranial radiation dose (<20 Gy TE OR=1.6,

p=.02; ≥20Gy TE OR=1.4, p=.01), leukemia diagnosis (TE OR=1.4, p=.02), or diagnosis age between 3-5 years (WM OR=1.4, p=.02) conferred higher risk for cognitive impairment compared to males with the same history. Females diagnosed with Hodgkin's lymphoma (Organization OR=0.61, p=.05) or non-Hodgkin's lymphoma (Organization OR=0.55, p=.03) were at lower risk for cognitive impairment compared to males.

Conclusions: We found sex-specific differences in rates of, and risk factors for, neurocognitive impairment, suggesting a sex vulnerability. Future studies examining interactions between sex hormones and treatment exposures during brain development will enable tailoring treatments follow-up interventions to ensure that quality of life is maximized.

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6 Graph Analysis of Resting State Functional Brain Networks and Associations with Cognitive Outcomes in Survivors on Pediatric Brain Tumor

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Objective: Adolescent and young adult survivors of pediatric brain tumors often live with long-term neuropsychological deficits, which have been found to be related to functional and structural brain changes related to the presence of the tumor itself as well as treatments such as radiation therapy. The importance of brain networks has become a central focus of research over recent decades across neurological populations. Graph theory is one way of analyzing network properties that can describe the integration, segregation, and other aspects of network organization. The existing literature using graph theory with survivors of brain tumor is small and inconsistent; therefore,