

Survivors Using the Neurological Predictor Scale and the Pediatric Neuro-Oncology Rating of Treatment Intensity

Alannah R Srsich¹, Matthew C Hocking^{1,2}

¹The Children's Hospital of Philadelphia, Philadelphia, PA, USA. ²Perelman School of Medicine at The University of Pennsylvania, Philadelphia, PA, USA

Objective: Pediatric brain tumor survivors (PBTs) represent a growing group of childhood cancer survivors vulnerable to adverse neuropsychological outcomes following treatment. Although the identification of risk factors has motivated the efforts to reduce the incidence of neuropsychological late effects in PBTs, most of the prior research on late effects has examined these risk factors on an individually selective basis. Given that tumor-directed treatments generally involve a multimodal approach, consisting of a combination of surgical resection, chemotherapy, and/or radiation, and that each patient may have varying degrees of neurological complications, research is needed that focuses on neurocognitive risk factors holistically. The Neurological Predictor Scale (NPS) measures neurological complications associated with neurocognitive risks (e.g., hydrocephalus) and the use of various tumor-directed treatment modalities (e.g., craniospinal radiation). The Pediatric Neuro-Oncology Rating of Treatment Intensity (PNORTI) measures the intensity of pediatric brain tumor treatments, but its association with neuropsychological late effects has not been well-established. The present study aims to 1) evaluate treatment intensity as a risk factor for the development of neuropsychological late effects; and 2) expand upon the validity and clinical utility of the NPS and PNORTI as predictive measures for the development of neuropsychological late effects in PBTs.

Participants and Methods: A retrospective chart review was completed of PBTs ($n = 167$, $M_{age} = 13.47$, $SD = 2.80$) who were at least 2 years from the end of tumor-directed treatment (surgery, chemotherapy, and/or radiation therapy) and without a multi-system genetic disorder or severe developmental delay prior to brain tumor diagnosis. Neuropsychological outcomes of interest (IQ, processing speed, working memory, verbal comprehension, and

perceptual reasoning) were analyzed in relation to the NPS and PNORTI.

Results: NPS scores ranged from 1 to 11 ($M = 5.58$, $SD = 2.28$) and PNORTI scores ranged from 1 ($n = 101$; 62.7%) to 3 ($n = 18$; 11.2%). Survivors were on average approximately 6 years post-treatment ($M = 6.13$, $SD = 3.39$). Pearson bivariate correlations revealed that NPS scores were significantly correlated with IQ ($r = -.20$, $p = .015$) and processing speed ($r = -.27$, $p = .015$). Models examining the predictive utility of the NPS on neuropsychological outcomes showed that, when controlling for age at diagnosis and sex, NPS scores significantly predicted IQ [$F(3, 147) = 10.83$, $p < .001$, $R^2 = .18$, $R^2_{adjusted} = .16$] and processing speed [$F(3, 88) = 5.62$, $p = .001$, $R^2 = .16$, $R^2_{adjusted} = .13$]. A one-way ANOVA showed no significant differences on neuropsychological outcomes based on PNORTI scores.

Conclusions: The findings suggest that the NPS has value in predicting IQ and processing speed above and beyond demographic variables. However, treatment intensity (PNORTI) was not associated with neuropsychological domains in our sample. Future longitudinal research should examine which specific neurological risk factors within the NPS account for the most variance in neuropsychological outcomes.

Categories: Cancer

Keyword 1: brain tumor

Keyword 2: neuro-oncology

Keyword 3: cognitive functioning

Correspondence: Alannah Srsich, The Children's Hospital of Philadelphia, srsicha@chop.edu

4 Relationships Between Task-Switching Performance and Adaptive Behavior Outcomes in Survivors of Pediatric Brain Tumor

Jordan E Pincus, Kylie A Szymanski, Tricia Z King
Georgia State University, Department of Psychology, Atlanta, GA, USA

Objective: Survivors of pediatric brain tumor (BT) experience impaired executive function (EF) and adaptive behavior (i.e. the ability to complete daily living tasks independently). The

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 ($p = .001$, $r^2_{\text{sempartial}} = .14$), Personal Living ($p = .002$, $r^2_{\text{sempartial}} = .13$), and Community Living ($p = .003$, $r^2_{\text{sempartial}} = .11$), 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 ($p = .036$, $r^2_{\text{sempartial}} = .06$) and Community Living ($p = .04$, $r^2_{\text{sempartial}} = .05$), 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

Keyword 1: brain tumor

Keyword 2: executive functions

Keyword 3: adaptive functioning

Correspondence: Jordan E Pincus, Georgia State University, Department of Psychology, Atlanta, GA, jpincus1@student.gsu.edu

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

Rachel K Peterson¹, Yan Chen², Kevin Oeffinger³, Yutaka Yasui⁴, Wendy Leisenring⁵, Gregory T Armstrong⁶, Leslie L Robison⁴, Rebecca M Howell⁷, Sogol Mostoufi-Moab⁸, Jordan Gilleland Marchak⁹, Kevin R. Krull⁴, Kim Edelstein¹⁰

¹Kennedy Krieger Institute, Baltimore, MD, USA.

²University of Alberta, Calgary, Canada. ³Duke University, Durham, NC, USA.

⁴St. Jude Children's Research Hospital, Memphis, TN, USA.

⁵Fred Hutch Cancer Research Center,