Neurocognitive outcomes in adult survivors of neuroblastoma: A report from the Childhood Cancer Survivor Study.

Caroline Hesko, Wei Liu, Deokumar Srivastava, Tara M. Brinkman, Lisa Diller, Todd M. Gibson, Kevin C. Oeffinger, Wendy Leisenring, Rebecca M. Howell, Gregory T. Armstrong, Kevin R. Krull, Tara O. Henderson; University of Chicago Comer Children's Hospital, Chicago, IL; St. Jude Children's Research Hospital, Memphis, TN; Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA; Duke University, Durham, NC; Fred Hutchinson Cancer Research Center, Seattle, WA; Department of Radiation Physics, The University of Texas MD Anderson Cancer Center, Houston, TX; The University of Chicago, Chicago, IL

Background: Long-term survivors of neuroblastoma may be at risk for neurocognitive impairment due to young age at diagnosis and intensive multimodal therapies. **Methods**: 837 survivors of neuroblastoma (57% female; median [range] age 25 [17-58] years, age at diagnosis 1 [0-21] years) and 728 siblings (56% female; age 32[16-43] years) self-reported neurocognitive problems using a neurocognitive questionnaire. Impairment was defined as scores ≥90th percentile of siblings in emotional regulation (ER), organization, task efficiency (TE), and memory. Multivariable log-binomial models evaluated associations with treatment exposures, era and chronic conditions (Grade 2-4 CTCAE v5) adjusting for sex, age, and race. Analyses were stratified by age at diagnosis (≤1 and > 1 year) as proxy for risk group. **Results:** Rates of impairment were 19.7% (ER), 25.3% organization, 21.9% TE and 19.4% for memory. Survivors had 50% higher risk of impaired TE (≤1 year relative risk [RR] 1.48, 95% confidence interval [CI] 1.08-2.03; > 1 year: RR 1.58, CI 1.22-2.06) and ER (≤1 year RR 1.51, CI 1.07-2.12; > 1 year RR 1.44, CI 1.06-1.95) versus siblings. Among survivors ≤1 year at diagnosis, treatment with platinum (RR 1.74, CI 1.01-2.97), hearing loss (RR 1.95, CI 1.26-3.00), cardiovascular (RR 1.83, CI 1.15-2.89) and neurologic (RR 2.00, CI 1.32-3.03) conditions were associated with higher risk of impaired TE. Female sex (RR = 1.54, CI, 1.02-2.33), cardiovascular (RR 1.71, CI 1.08-2.70) and respiratory (RR 1.99, CI 1.14-3.49) conditions were associated with higher risk of impaired ER. Among survivors > 1 year at diagnosis those treated in 1970-79 vs. 1990-99 had 80% higher risk of impaired ER (RR 1.77, CI 1.02-3.06). Hearing loss (RR 1.56 (1.09-2.24), respiratory (RR 2.35, CI 1.60-3.45) and cardiovascular (RR 1.74, CI 1.12-2.69) conditions were associated with higher risk of impaired TE. **Conclusions**: Adult survivors of neuroblastoma are at-risk for neurocognitive impairment. Differences associated with age at diagnosis, chronic disease and treatment exposures may inform risk-stratified inventions to improve neurocognitive outcomes. Reduced risk in later eras may reflect improved supportive care and knowledge of late effects.