Neurosensory deficits and functional outcomes in childhood cancer survivors: A report from the Childhood Cancer Survivor Study (CCSS)

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Background: Survivors of childhood cancer are at risk for neurosensory deficits secondary to their disease and treatment. Previous research has characterized system-specific (e.g., visual) impairments; however, the prevalence of multisystem neurosensory deficits and their functional impact remain unknown.

Methods: Adult 5-year survivors (n=20037, median age 36 [range 18-69] years, 53.4% male) and sibling controls (n=4121) reported neurosensory deficits related to vision, hearing, vestibular, and neuropathy. Comorbidities were graded using modified CTCAE v5 and defined as having at least one grade 1 neurosensory deficit in one, two, and three/four systems. Survivors reported neurocognitive function (CCSS Neurocognitive questionnaire; impairment: <10th %ile of sibling distribution), emotional distress (BSI-18; impairment: T score ≥63), quality of life (SF-36; impairment: T score <40), and functional independence. Multivariable models estimated the prevalence of neurosensory comorbidities, adjusted for age, sex, and race. Multivariable models further adjusted for other chronic conditions and neurotoxic therapies examined associations between comorbidities and functional outcomes in survivors.

Results: Survivors had higher prevalence of neurosensory deficits in one (31% vs. 24%; prevalence ratio [PR] 1.4, 95% confidence interval [CI] 1.3-1.5), two (14% vs. 8%; 2.2, 1.9-2.5) and three/four systems (9% vs. 3%; 3.3, 2.9-4.1) than siblings. Neurosensory comorbidities were associated with greater risk of neurocognitive impairment (task efficiency and memory), emotional distress (anxiety) and poor quality of life (physical and social function) in a dose-dependent manner in survivors (Table). Similar effects were observed for indicators of functional independence: assistance with personal care/routine needs (one system: relative risk [RR] 2.7, 95% CI 2.2-3.3; two systems: 4.1, 3.3-5.0; three/four systems: 6.5, 5.4-7.9), interference with job/school (2.5, 2.2-3.0; 3.8, 3.2-4.5; 6.1, 5.2-7.1), no driver's license (1.5, 1.3-1.8; 2.4, 2.1-2.8; 3.8, 3.2-4.4), and non-independent living (1.3, 1.2-1.4; 1.8, 1.6-2.0; 2.1, 1.9-2.4).

Conclusions: Adult survivors of childhood cancer have high rates of comorbid neurosensory deficits that have a dose-dependent impact on functional outcomes. Survivors with multisystem deficits should be prioritized for interventions to support functional independence.

Table. Relative risk (95% CI) of impaired outcomes in survivors with neurosensory comorbidities

Neurosensory comorbidities (# organ systems)	Memory	Task Efficiency	Anxiety	Physical Function	Social Function
0 (ref.)	-	-	-	-	-
1	1.6 (1.4-1.8)	1.8 (1.6-2.0)	2.6 (2.2-3.1)	2.2 (1.9-2.6)	1.9 (1.7-2.1)
2	2.2 (2.0-2.5)	2.4 (2.2-2.7)	3.4 (2.8-4.1)	3.1 (2.7-3.5)	2.5 (2.2-2.8)
3/4	3.1 (2.7-3.4)	3.3 (3.0-3.7)	5.2 (4.4-6.3)	4.4 (3.8-5.0)	3.2 (2.9-3.7)

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