

Neurocognitive impairment and functional independence in adult survivors of childhood glioma: A report from the Childhood Cancer Survivor Study (CCSS)

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Abstract (300/300 words):

Purpose: Survivors of pediatric glioma are at risk of developing physical and neurocognitive sequelae secondary to their tumor and its treatment. The contribution of these conditions to attainment of functional independence has not previously been examined.

Methods: 1,284 adult survivors of pediatric glioma (48% male, median [range] 30 [18-51] years at assessment, 22 [15-34] years since diagnosis) completed the CCSS Neurocognitive Questionnaire with impairment defined as scores > 90th %ile of sibling norms. Treatment exposures were categorized as surgery only, chemotherapy (\pm surgery), or cranial radiation (\pm chemotherapy/surgery). Self-reported chronic health conditions (CHCs) were graded by organ system using NCI's CTCAE v4.3. Latent class analysis utilized six factors (employment, marital status, independent living, driver's license, assistance with routine needs, assistance with personal care needs) to identify classes of functional independence. Multivariable modified Poisson regression evaluated relative risk (RR) of neurocognitive impairment between the classes, adjusting for sex, race, age at assessment, and age at diagnosis. Path analysis explored the impact of treatment exposures on functional independence, mediated by Grade 2-4 CHCs and neurocognitive impairment.

Results: Three latent classes of functional independence were identified: independent (58%), moderately independent (20%), and non-independent (22%). Compared to the independent class, non-independent survivors were at elevated risk for impaired task efficiency (RR=3.86, 95% CI, 2.97-5.01), memory (RR=2.39, 95% CI, 1.91-2.98), organization (RR=2.04, 95% CI, 1.64-2.54), and emotional regulation (RR=1.67, 95% CI, 1.30-2.15). Path analysis revealed significant direct paths from cranial radiation ($\beta=0.14$), impaired task efficiency ($\beta=0.42$), and sensorimotor ($\beta=0.22$) and endocrine conditions ($\beta=0.24$) to non-independence. Cranial radiation also was indirectly associated with non-independence through impaired task efficiency ($\beta=0.06$), and sensorimotor ($\beta=0.06$) and endocrine conditions ($\beta=0.10$).

Conclusions: Neurocognitive impairment and chronic health conditions partially mediate the association between treatment exposures and attainment of independence in adulthood, identifying potential intervention targets to promote independence in long-term survivors.