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Ototoxicity and Cognitive Outcomes among Very Young Children Treated for Brain Tumors: Findings from a Multisite, Prospective, Longitudinal Trial

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Abstract

Background: Brain tumor treatment can result in sensorineural hearing loss (SNHL) that is associated with cognitive declines in school-age children. Young children treated for brain tumors are at heightened cognitive risk. This study examines the unique contribution of treatment-related ototoxicity to cognitive outcomes in young children treated for brain tumors.

Methods: 135 young children (mean age= 1.7 years) with a newly diagnosed malignant brain tumor were treated with chemotherapy, with or without focal proton or photon radiation therapy. Serial audiology and neurocognitive assessments were conducted for five years as part of a prospective, multisite, longitudinal trial (SJYC07; [NCT00602667](#)). SNHL was dichotomized as present versus not present (Chang grade $\geq 1a$ vs. 0). Neurocognitive assessments included intellectual functioning and parent ratings of adaptive functioning and attention.

Results: 67% of patients experienced mild-to-severe SNHL, which was associated with younger age at diagnosis ($p < .001$) but not sex, treatment, or study risk arm ($p > .10$). Pre-treatment, higher IQ was associated with older age and higher socioeconomic status ($p < .01$), with a negative change in IQ trajectory after SNHL that was worse for children with supratentorial tumors. Pre-treatment, higher adaptive functioning was associated with older age ($p = .0001$), with a negative change in adaptive functioning trajectory after SNHL that was worse for those treated at a younger age. Attention problems increased after SNHL for the entire group ($p = .0099$).

Conclusions: SNHL is associated with IQ decline and worsening adaptive functioning and attention in young children treated for brain tumors. These findings have important implications for treatment modifications, interventions, and caregiver education.

Keywords: brain tumor; cognitive outcomes; ototoxicity; pediatric oncology; young child.

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