

Chemotherapy-induced hearing loss affects cognition in pediatric brain tumor survivors

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than in the past, thanks to the use of intense treatments using platinum-based chemotherapy (cisplatin and high-dose carboplatin). Unfortunately, the therapy has a known side effect of permanent hearing loss, resulting from damage to the inner ear. Investigators at Children's Hospital Los Angeles now report that this type of chemotherapy may not only impact hearing, but that the hearing loss may then contribute to longterm neurocognitive deficits.

The study will be published online on Nov. 3 in the journal Pediatric Blood & Cancer.

"Neurocognitive effects are associated with radiation therapy for brain tumors; however, the use of platinum-based chemotherapy regimens to reduce or eliminate radiation therapy were thought to spare these harmful side effects to the brain, despite their known impact on hearing," said Etan Orgel, MD, MS, attending physician at CHLA and principal investigator on the study. "Our research suggests that, despite this practice shift in therapy, the impact of hearing loss itself in brain tumor survivors leads to long-term neurocognitive problems."

In both the general pediatric population and among children with non-brain related tumors, even mild hearing loss has been associated with declines in academic performance and language acquisition. However, recent studies did not specify the exact parameters of such declines, and included only a brief follow-up period. The CHLA researchers suspected that a longer follow-up period might reveal greater information about the true neurocognitive impact, as well as specific areas affected.

Their retrospective analysis involved patients under the age of 21 years old who were treated for malignant brain tumors at Children's Hospital Los Angeles or Miller Children's & Women's Hospital

More children are surviving malignant brain tumors Long Beach. Treatment included platinum-based chemotherapy as well as a broad array of regimens, including radiation therapy and/or bone marrow transplantation. Care at the two participating institutions included comprehensive screening for late-effects—health problems that develop as a result of cancer therapy-inclusive of neurocognitive and audiological changes.

> For purposes of this study, the presence of sensorineural hearing loss was determined as a level consistent with a patient's need for a hearing aid after treatment. Developmentally appropriate neuropsychological testing included evaluation of intelligence, executive function, memory, visualmotor integration and achievement. Time from diagnosis to audiology testing was two to three years, and the interval for neurocognitive testing was four to five years from start of treatment. Patients who received radiation therapy were balanced between the two groups—individuals with and without hearing loss.

> Among brain tumor survivors treated with platinumbased therapies, 55 percent sustained sensorineural hearing loss. Independent of radiation therapy effects, patients who experienced hearing loss were found to have significant deficits in intelligence, executive function, and verbal reasoning skills.

The study indicates that children who received radiation therapy and developed hearing loss are at particularly high-risk for neurocognitive decline. The report also strongly suggests that even children spared radiation therapy who develop hearing loss are at high risk for severe deficits and warrant similar neurocognitive monitoring and potential intervention.

"This is the first report to reveal the specific pattern of hearing loss-associated deficits, pointing to a serious risk for cognitive dysfunction, daily difficulties, and poorer lifetime achievement," Orgel



added. "Armed with this information, we can begin to take steps to mitigate the effects of hearing loss resulting from platinum-based chemotherapy, through early intervention and developing appropriate strategies for neurocognitive rehabilitation."

"As we work to develop more effective treatments for children with cancer, we are ever mindful of the side effects associated with these therapies," said Alan S. Wayne, MD, director of the Children's Center for Cancer and Blood Diseases at CHLA. "Our physicians are monitoring their patients for signs of adverse effects of therapy, and CHLA researchers are working to develop strategies to counteract, and ultimately prevent, those effects."

More information: *Pediatric Blood & Cancer*, onlinelibrary.wiley.com/doi/10 ... 2/pbc.25804/abstract

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