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Effect of sensorineural hearing loss on neurocognitive and adaptive functioning in survivors of pediatric embryonal brain tumor

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Abstract

Purpose: Survivors of pediatric embryonal brain tumors (BT) are at high risk for sensorineural hearing loss (SNHL) associated with neurocognitive decline. However, previous studies have not assessed the relationship between SNHL and adaptive functioning. We examined neurocognitive and adaptive functioning in patients with and without SNHL.

Methods: Participants included 36 patients treated for an embryonal BT with craniospinal irradiation (CSI) and cisplatin chemotherapy who were assessed 6.7 years post-treatment on average. The impact of SNHL on neurocognitive performance and parent-rated adaptive functioning was assessed in univariate and multivariate analyses.

Results: There were 17 cases with SNHL (mean age at evaluation = 14.4) and 19 cases with NH (mean age at evaluation = 13.8). After accounting for age at diagnosis and additional covariates in multivariable analyses, SNHL was associated with worse overall intellectual functioning ($p = 0.027$) and perceptual reasoning ($p = 0.016$) performance. There was no effect of SNHL on adaptive functioning in multivariable models. Age at diagnosis and sex were associated with performance on neurocognitive measures.

Conclusions: SNHL in pediatric embryonal BT is associated with increased risk for neurocognitive deficits in conjunction with other demographic and treatment-related factors.

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Keywords

Embryonal brain tumor; medulloblastoma; pediatric; sensorineural hearing loss; cognitive; adaptive

Introduction

Treatment for pediatric embryonal brain tumors (BT) typically involves surgery, radiation therapy (RT), and chemotherapy [1, 2]. With improving survival rates, there has been increased focus on the functional (e.g. intelligence, academic achievement) outcomes of these children [3, 4]. Survivors of pediatric embryonal BTs are at risk for neurocognitive deficits involving reasoning, memory, attention, working memory, processing speed, and motor coordination [5–7]. These effects often emerge several years post-treatment and persist throughout adulthood. Younger age at RT [5–7], greater treatment intensity [6, 7] (e.g. higher RT dose, larger RT field), and posterior fossa syndrome [8] are additional risk factors for neurocognitive dysfunction. Beyond these cognitive difficulties, survivors of pediatric embryonal BT display adaptive deficits, involving difficulties completing activities of daily living [9].

Certain chemotherapy agents [10, 11] and cranial RT [12, 13] are associated with ototoxicity, which can manifest as permanent and progressive sensorineural hearing loss (SNHL). Chemotherapy regimens for embryonal BT typically rely on platinum-based agents that cross the blood-brain barrier and penetrate the inner ear, which can cause damage to the cochlea [14]. RT, independent of chemotherapy, has also been associated with the development of SNHL [13] due to radiation-induced cochlear damage if the cochlea is within the radiation field [15]. Cisplatin based ototoxicity is typically bilateral [10]. However, ototoxicity resulting from RT can often be unilateral due to higher radiation dosage to a single ear [13, 16], particularly with newer treatment protocols utilizing boosts to the tumor bed rather than the full posterior fossa. Rates of SNHL in children with embryonal BT treated with chemotherapy and RT range from 15 to 25%, with greater rates of SNHL found at longer term follow-up [5, 16, 17].

Hearing loss is linked to changes in cognitive functioning across the lifespan stemming from its associations with language development and overall brain integrity [18, 19]. Children who are deaf or hard of hearing - without cancer - display cognitive weaknesses compared to their normal hearing (NH) peers even after excluding children who have an intellectual disability [20]. Weaknesses are observed in aspects of perceptual reasoning, attention, and executive functioning skills [21–23], with greatest deficits noted in language skills [24]. These difficulties are observed not only in children who have bilateral hearing loss, but in children with unilateral (only one ear) hearing loss as well [25, 26]. Adaptively, children with congenital hearing loss without an intellectual disability display deficits in daily-living skills [20]. In a group of deaf children being considered for cochlear implantation, Kushalnagar and colleagues found a strong positive relationship ($r = 0.65$) between intelligence and adaptive behavior [27]. These results are relatively consistent with previous reports for individuals with NH, with correlations ranging from 0.40 to 0.60 [28].

However, in pediatric BT patients and many other clinical groups (e.g. attention deficit/hyperactivity disorder, autism) there is often a discrepancy between intellectual ability and adaptive functioning due to the influence of other neuropsychological domains (e.g. executive functioning, fine motor control) that may limit an individual's capacity to fully utilize otherwise intact intellectual reasoning skills [29–31]. Therefore, it is important to assess adaptive skills in addition to cognitive ability to fully capture a patient's level of functional independence in daily life. Additionally, these adaptive skills may be more amenable to intervention, although there is a paucity of research in this area.

To date, studies have examined the relationship between ototoxicity and neurocognitive outcomes in survivors of embryonal BT [32, 33], medulloblastoma [5], or multiple types of BTs [34] up to approximately 5 years post-treatment [5, 32–34]. Children with severe SNHL showed greater decline in global reasoning [5, 32, 34], academic achievement [5, 33, 34], phonetic processing [33], processing speed [33, 34], and memory [34] compared to children with mild-to-moderate SNHL or NH. Neurocognitive differences were examined after accounting for age at diagnosis [33, 34], time since diagnosis [5, 34], and other clinical factors (e.g. posterior fossa syndrome, radiation dose) [32–34]. However, to our knowledge, studies have not examined the relationship between SNHL and adaptive outcomes in survivors of pediatric embryonal BT.

The primary objective of this paper was to determine the relationship between SNHL and long-term cognitive and adaptive functioning in pediatric embryonal BT patients treated with craniospinal irradiation (CSI) and cisplatin chemotherapy. We addressed the following: a) differences in cognitive and adaptive functioning in pediatric embryonal BT patients with and without SNHL; b) demographic and clinical predictors of performance; and c) relationships between cognitive and adaptive functioning in children with and without SNHL. We hypothesized that those with SNHL would perform worse than those with NH on all cognitive and adaptive domains. We predicted greater cognitive and adaptive deficits for younger children at diagnosis and for those who received more intensive treatment (e.g. CSI dose and total RT dose). Finally, we predicted there would be a strong relationship between cognitive and adaptive functioning in both the NH and SNHL groups, consistent with the general population.

Methods

Participants

Participants were part of a larger study examining long-term neurocognitive, social-emotional, and adaptive outcomes in survivors of pediatric BT. Patients were approached for enrollment based on consecutive outpatient appointments with the medical team. In the present cross-sectional study, we examined outcomes of patients (1) diagnosed with medulloblastoma, primitive neuroectodermal tumor, or pineoblastoma between 1996–2015. Patients were (2) 18 years old at diagnosis, (3) received CSI and cisplatin chemotherapy, (4) underwent an audiological evaluation, (5) and participated in a cognitive evaluation at least two years post-CSI. All patients were (6) between 5–20 years old at evaluation.

Fifty-one patients met initial inclusion criteria. We excluded patients who did not have an audiological evaluation prior to their cognitive evaluation (n=3). We further excluded patients without relevant cognitive/adaptive testing data (n=3). Finally, we excluded patients with a FSIQ below 60 (n=9), due to global cognitive impairment limiting the interpretability of results, resulting in a sample of 36 patients. The sample included 34 cases with medulloblastoma, 1 pineoblastoma, and 1 cerebral primitive neuroectodermal tumor.

Audiology Assessments

Audiometric evaluations using tympanometry, pure-tone air and bone conduction thresholds, auditory brainstem response, auditory steady-state response, and/or distortion-product otoacoustic measurements were abstracted from medical records of eligible patients. Data were assigned ototoxicity grades using the Chang Ototoxicity Grading Scale [35], consistent with previous research [5, 34]. Chang scores $\geq 2b$ were considered cutoffs for SNHL in the present study. Patients received a median of 9 (range 1–17) audiological assessments over the course of their treatment and follow-up. A single audiogram was included in analyses that demonstrated greatest impairment in hearing prior to the cognitive assessment. The selected audiogram was based on the following criteria applied in sequence (i.e. if multiple audiograms met the same Chang rating on the first criteria, the second criteria was applied): (1) worst (highest grade on the scale) Chang score for the worse ear and (2) most recent audiogram prior to the cognitive assessment. We combined groups with bilateral (n=12) and unilateral (n=5) hearing loss, as we lacked sufficient power to assess either in isolation and because of the documented associations between cognitive deficits and unilateral hearing loss in non-cancer pediatric populations [26].

Measures

Adaptive Functioning.—Adaptive functioning was assessed using the Adaptive Behavior Assessment System, Second Edition (ABAS-II) [36], or Third Edition (ABAS-3) [37] Parent Form. The Global Adaptive Composite (GAC), Conceptual (communication, functional academics, self-direction), Social (social skills, leisure activities), and Practical (self-care, home/school living, community use, health and safety) scores were employed in this study. The ABAS-II and ABAS-3 are highly correlated: corrected r for GAC=.88 and corrected r 's for adaptive domains ranged from .83 to .87 [37].

Intellectual Functioning.—Participants were administered the age-appropriate version of the Wechsler Scales of Intelligence [38–42]. The Full-Scale IQ (FSIQ) score provides a measure of global intellectual functioning. Index scores include: Verbal Comprehension (VCI), Perceptual Reasoning (PRI)¹, Working Memory (WMI), and Processing Speed (PSI). The VCI measures verbal reasoning ability. The PRI measures nonverbal and fluid reasoning ability. The WMI measures the ability to store and manipulate information in short-term memory. The PSI measures the speed, efficiency, and accuracy of information processing.

¹The Wechsler Intelligence Scale for Children, Fifth Edition (WISC-V) does not generate a PRI score. At our request, NCS Pearson Inc. (publisher of the WISC-V) generated the norms for calculating PRI scores from WISC-V subtests to enable comparison of scores across versions. WISC-V PRI reliabilities ranged from .93-.95 across ages 6–16 [50].

Statistical Analyses

Demographic and clinical factors were compared in those with (Chang $\geq 2b$ in worse ear) and without (Chang $< 2b$ in worse ear) SNHL using Chi Square, Fisher exact test, or independent t -tests, as appropriate. Differences in neurocognitive and adaptive composite standard scores were assessed between the SNHL and NH groups using independent t -tests. Cohen's d effect sizes were calculated for group comparisons. Individual multivariate linear regression models were built upon a base model including age at diagnosis [5, 6] and presence or absence of SNHL. Additional candidate predictors were then added to each model if $p < 0.05$ in univariate analyses (based on bivariate Pearson, point-biserial, and Spearman's Rho correlations for appropriate data types).

To assess the relationship between neurocognitive and adaptive functioning, we ran bivariate Pearson correlations between the FSIQ and ABAS-3 GAC for the SNHL and NH groups. We assessed if SNHL status moderated the relationship between the FSIQ and GAC indices using the PROCESS macro for SPSS [43].

Results

Demographic and Clinical Characteristics

Comparison of demographic and clinical characteristics between groups with (Chang $\geq 2b$ in worse ear) and without (Chang $< 2b$ in worse ear) SNHL are displayed in Table 1. No significant differences were observed between the groups on any demographic or clinical characteristics ($p > 0.05$). Correlations between demographic and clinical predictors with outcome measures are displayed Table 2.

Frequency of Sensorineural Hearing Loss

Chosen audiograms were administered a median of 4.8 years after CSI (range=0.5–12.8 years). When using audiogram data for the worse ear (e.g. combining bilateral and unilateral SNHL), there were 17 cases with SNHL (Chang $\geq 2b$, 47%) and 19 cases with NH (Chang $< 2b$, 53%). As expected, none of the children in the NH group were wearing a hearing aid at the time of their audiogram, whereas 11 of the 17 (65%) children with SNHL were wearing a hearing aid.

Neurocognitive Outcomes

Overall, the sample received cognitive assessments a median of 6.7 years after CSI (range=2.3–15.2 years). There was a moderate to large effect of SNHL on all neurocognitive indices (all effect sizes > 0.5), with the largest effect observed on the PRI ($d = 0.94$). Only group differences on the VCI, PRI, and FSIQ reached statistical significance (all $p < 0.05$). Differences in neurocognitive performance scores between the SNHL and NH groups are displayed in Table 3.

Regression analyses for the neurocognitive indices are presented in Table 4. After adjusting for other factors, the presence of SNHL remained a significant predictor of FSIQ ($p = 0.019$) and PRI ($p = 0.016$) scores. SNHL was not significantly associated with the VCI ($p = 0.107$), WMI ($p = 0.225$), and PSI ($p = 0.138$) after adjusting for covariates. Younger age at diagnosis

was associated with poorer performance on the VCI, WMI, and FSIQ ($p < 0.05$). Males performed worse on the WMI ($p = 0.002$) and FSIQ ($p = 0.006$). Patients with posterior fossa syndrome obtained lower scores on the WMI ($p = 0.010$).

Adaptive Outcomes

Differences in parent reported adaptive ratings between the SNHL and NH groups are displayed in Table 3. There was a moderate, though not statistically significant, effect of SNHL on parent-rated adaptive skills on the Conceptual ($d = 0.62$) and GAC ($d = 0.46$) indices. There were no significant differences in parent ratings on the Social ($p = 0.171$) or Practical ($p = 0.430$) indices between the groups.

Regression analyses for the adaptive indices are presented in Table 5. After adjusting for covariates, there were no significant associations between SNHL and parent-rated adaptive functioning on the Conceptual, ($p = 0.173$), Social ($p = 0.400$), Practical ($p = 0.454$), or GAC ($p = 0.207$) indices.

Association between Neurocognitive and Adaptive Outcomes

There was a trend towards a positive correlation between neurocognitive (FSIQ) and adaptive (GAC) functioning ($r(15) = 0.47$, $p = 0.059$) in the SNHL group, but a weaker relationship in the NH group ($r(17) = 0.14$, $p = 0.563$). Yet, SNHL status did not significantly moderate the relationship between the FSIQ and GAC indices ($p = 0.255$).

Discussion

Children treated for an embryonal BT with CSI and chemotherapy are at high risk for SNHL, as evidenced by 33% of our sample displaying bilateral severe SNHL several (median = 4.8) years after treatment. A smaller percentage (14%) demonstrated severe unilateral hearing loss. The high rates of SNHL suggest a need to assess how SNHL is associated with other areas of functioning, particularly functioning in day-to-day activities.

Consistent with our hypotheses, those with SNHL displayed greater neurocognitive deficits than those with NH and there was a moderate effect of SNHL on conceptual (e.g. language, communication, reading, writing, number concepts, and self-direction) adaptive functioning. Notably, this is the first study to examine adaptive deficits associated with SNHL in children with BTs or to assess long-term outcomes, occurring on average 6 ½ years following CSI. Several of the neurocognitive effects persisted after controlling for medical and demographic covariates.

Demographic and clinical predictors accounted for a small percentage of the variance in overall adaptive outcomes among embryonal BT patients. In univariate analyses, there was a moderate effect of SNHL on parent-rated conceptual adaptive functioning. Given the impact of hearing loss on language functioning and academic skills [25, 44], it is not surprising that pediatric BT survivors, who are already susceptible to weaknesses in these domains, are potentially further affected by SNHL. However, this association did not persist in multivariate analyses. Clinician or teacher ratings of adaptive functioning may provide additional insight into adaptive functioning. Previous research has demonstrated that teacher

ratings are more sensitive to deficits in executive functioning skills than parent ratings in patients with a pediatric BT [45].

Consistent with Orgel and colleagues (2016), we found that the group with SNHL performed below expectations across several neurocognitive indices. The largest group differences were observed on measures of perceptual and visuospatial reasoning (PRI) rather than verbal outcomes (VCI). The literature in deaf and hard of hearing populations has consistently demonstrated language deficits in those impacted by hearing loss [24], likely due to the negative impact of impaired hearing on vocabulary and speech development. Yet, several studies have also demonstrated an association between hearing loss and visuospatial skills [23, 26]. Specific language deficits may not be as apparent for children with treatment induced hearing loss that occurs later in childhood, often after critical stages of language development [46]. Future research with larger samples should investigate if the timing of HL alters how specific neurocognitive skills are affected. The neurocognitive deficits associated with SNHL are likely not fully due to hearing loss causing cognitive changes in specific domains (e.g. hearing loss limiting vocabulary development). Rather, SNHL in patients with a pediatric BT likely represents overall neurocognitive/brain integrity and the shared impact of treatment on both neurocognitive functioning and hearing loss.

Unlike previous studies assessing the relationship between ototoxicity and cognitive outcomes [5, 32–34], we included children with unilateral hearing loss in our SNHL group. The functioning of the better ear likely represents a patient's best potential hearing status. Yet, many studies in the deaf and hard of hearing population have demonstrated deficits in speech, language, and overall cognition in children with unilateral hearing loss [25, 47]. Children with unilateral hearing loss likely require an aggressive approach to treatment to potentially limit neurocognitive changes. Further study of neurocognitive and adaptive outcomes in patients with unilateral hearing loss is needed to better understand how these patients differ from those with bilateral hearing loss and associated treatment considerations (e.g. need for hearing aids or accommodations for school).

In contrast to adaptive outcomes, demographic and clinical predictors accounted for 50% of the variance in overall cognitive functioning (FSIQ). Younger age at diagnosis and posterior fossa syndrome were associated with poorer neurocognitive outcomes, consistent with findings in the pediatric BT literature [5, 6, 48]. We also found that male sex was associated with poorer performance on the WMI and FSIQ. Yet, it is important to note that the observed sex differences were based on a small sample, including only 8 females. A review of this literature suggested that there is support for a female vulnerability to cognitive late effects in acute lymphoblastic leukemia but not in brain tumor patients [49].

Although not reaching statistical significance, our findings suggest there may be differences in the relationship between cognitive and adaptive functioning in children with and without SNHL. Prior studies in children with BTs have demonstrated weak correlations between cognitive and adaptive functioning [29, 31]. These studies suggested cognitive testing tends to measure maximal ability, whereas adaptive ratings reflect application in daily life [30]. In our sample, similar results were found for children with NH.. Yet, for those with SNHL,

there was a moderate positive correlation between the FSIQ and GAC. These associations potentially reflect the impact of hearing loss on adaptive functioning in isolation.

The current study has several strengths including use of a standardized assessment battery and availability of long-term follow up. Overall, the results presented are preliminary in nature due to several study limitations. Due to small sample size, we lacked the power to explore group differences in bilateral and unilateral hearing loss and, perhaps, were underpowered to detect effects of SNHL on adaptive functioning. Documentation of hearing aid usage and/or rationale for prescribing a hearing aid were not reliably documented. We utilized a cross-sectional study design, limiting our ability to determine the trajectory of functioning over time. Additionally, there was variability in the timing of both cognitive and audiological assessments across patients, potentially limiting the interpretability of the results. Finally, our cognitive and adaptive outcome measures were limited. Adaptive functioning was solely based on parent report, and the cognitive assessment battery was limited to overall IQ and component indices. Future studies should utilize multiple raters of adaptive functioning and specific language or reading measures that might be more sensitive to the effects of SNHL.

Conclusions

Embryonal BT patients are at high-risk for treatment-induced SNHL, which may be associated with neurocognitive and adaptive deficits. The observed deficits likely represent overall brain integrity and the shared impact of treatment on both neurocognitive functioning and hearing loss. Future research should examine additional treatment factors associated with SNHL to help further elucidate the mechanisms driving these associations. In addition, careful documentation of aided devices and their usage is needed to determine the effects of hearing aids on cognitive and adaptive functioning.

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TABLE 1

Demographic and clinical characteristics by hearing status

	Normal Hearing (n = 19)		Hearing Loss ^a (n = 17)		<i>p</i>
	<i>n</i>	%	<i>n</i>	%	
Sex					0.236
Male	13	68	15	88	
Female	6	32	2	12	
Race/Ethnicity					0.320
White	11	58	8	47	
Black	4	21	1	6	
Hispanic/Latino	3	16	6	35	
Other	1	5	2	12	
Maternal Ed.					0.370
4-year degree	10	53	5	29	
Some college	3	16	4	24	
No college	6	31	8	47	
Shunt					0.706
Yes	4	21	5	29	
No	15	79	12	71	
PFS					0.516
Yes	8	42	9	53	
No	11	58	8	47	
Amifostine					0.676
Yes	8	42	6	35	
No	11	58	11	65	
SCT					0.813
Yes	13	68	11	65	
No	6	32	6	35	
	Mean (sd)	Min-Max	Mean (sd)	Min-Max	<i>p</i>
Maximum Tumor Diameter (cm)	4.6 (1.0)	2.5 – 6.6	5.1 (0.9)	3.0 – 6.1	0.122
Total RT Dose to Tumor (Gy)	54.7 (1.2)	51.0 – 55.8	53.3 (5.1)	45.0 – 55.8	0.557
Craniospinal RT Dose (Gy)	25.6 (0.6)	15.0 – 36.0	25.4 (0.5)	18.0 – 36.0	0.923
Cisplatin Dose (mg/m ²) ^b	320.6 (76.7)	228 – 563	286.7 (77.0)	146 – 420	0.203
Age at Diagnosis (years)	7.4 (3.6)	2.2 – 15.4	6.9 (3.6)	2.3 – 12.3	0.675
Age at Audiogram (years)	11.6 (3.5)	5.5 – 17.5	12.8 (2.7)	8.1 – 17.5	0.288
Age at Cognitive (years)	14.4 (3.6)	7.7 – 19.7	13.8 (3.2)	9.2 – 19.6	0.592
Time from RT (years)	6.8 (3.5)	2.2 – 13.6	6.6 (3.6)	2.3 – 15.2	0.843

Note. Abbreviations: Ed = education, PFS = posterior fossa syndrome, RT = radiation therapy, SCT = stem cell transplant. Group comparisons based on Chi Square, Fisher exact test, or independent *t*-test, as appropriate.

^aHearing Loss based on worse ear Chang 2b.

^bMissing cisplatin dose data on a single case in the SNHL group.

TABLE 2

Univariate correlations between predictors with cognitive and adaptive outcomes

	VCI	PRI	WMI	PSI	FSIQ	Conceptual	Social	Practical	GAC
Sex ^a	.354 *	.376 *	.560 **	0.289	.508 **	.354 *	0.170	0.213	0.263
Race/Ethnicity ^b	−0.012	−0.187	0.122	0.003	−0.055	−0.133	−0.237	−0.135	−0.173
Maternal Education ^c	0.346 *	0.202	0.256	0.016	0.287	0.229	0.336 *	0.138	0.126
Shunt	0.136	−0.069	−0.088	−0.243	−0.017	−0.142	−0.190	−0.244	−0.248
PFS	−0.036	−0.018	−0.240	−.433 **	−0.189	−0.219	−0.035	−0.132	−0.162
SCT	0.206	.358 *	0.232	−0.048	0.270	0.232	0.306	0.099	0.223
Tumor Diameter (cm)	−0.228	−0.281	−0.277	0.010	−0.264	−0.184	−0.184	−0.219	−0.245
Total RT Dose (cGy)	0.309	0.316	0.197	0.058	0.284	0.131	0.064	0.057	0.087
CSI Dose (cGy)	−0.147	−0.070	−0.049	0.074	−0.097	0.186	0.130	0.192	0.188
Cisplatin Dose (mg/m ²) ^d	0.106	−0.002	−0.090	0.115	0.027	0.137	−0.068	−0.027	−0.002
Age at Diagnosis (yrs)	.380 *	.449 **	.383 *	0.120	.440 **	0.216	0.218	0.081	0.180
Time from RT (yrs)	−0.289	−0.130	−0.162	−0.199	−0.214	0.022	−0.205	−0.054	−0.071
Age at Cognitive (yrs)	0.086	0.298	0.246	−0.066	0.225	0.254	0.027	0.057	0.134
SNHL ^e	−.360 *	−.437 **	−0.305	−0.288	−.437 **	−0.304	−0.159	−0.136	−0.227

Note.

*
 $p < 0.05$,**
 $p < 0.01$.

Abbreviations: VCI = Verbal Comprehension Index, PRI = Perceptual Reasoning Index, WMI = Working Memory Index, PSI = Processing Speed Index, FSIQ = Full Scale Intelligence Quotient, GAC = Global Adaptive Composite, PFS = posterior fossa syndrome, SCT = stem cell transplant, RT = radiation therapy, cGy = centigray, CSI = craniospinal irradiation, SNHL = sensorineural hearing loss. For categorical predictors, absence of the condition was used as the reference group.

^a Male used as the reference level.^b Race/ethnicity split into two groups: non-Hispanic and Hispanic. Non-hispanic used as the reference level.^c Maternal education split into three levels: no college, some college, 4-year degree or more.^d Missing data on a single case in the SNHL group.^e Hearing Loss based on worse ear Chang 2b.

TABLE 3

Cognitive and adaptive outcomes by hearing loss status

Outcomes	Normal Hearing (n = 19)		Hearing Loss (n = 17)			
Neurocognitive scores	Mean (SD)	Min-Max	Mean (SD)	Min-Max	<i>p</i>	<i>d</i>
VCI	98.0 (14.1)	76 – 136	87.4 (14.3)	69 – 119	0.031	0.74
PRI	102.5 (16.0)	77 – 135	88.7 (12.9)	67 – 108	0.008	0.94
WMI	93.5 (16.7)	65 – 122	83.6 (14.9)	59 – 113	0.071	0.62
PSI	81.8 (11.8)	65 – 108	74.8 (12.4)	53 – 100	0.089	0.57
FSIQ	93.9 (15.4)	75 – 134	80.7 (12.2)	62 – 107	0.008	0.95
Adaptive scores						
Conceptual	94.6 (14.2)	67 – 120	86.2 (12.7)	53 – 105	0.071	0.62
Social	94.5 (14.2)	60 – 120	90.2 (13.2)	58 – 116	0.356	0.31
Practical	92.1 (16.5)	60 – 120	87.9 (14.5)	50 – 120	0.430	0.27
GAC	93.0 (14.6)	63 – 120	86.4 (14.4)	49 – 119	0.182	0.46

Note. Abbreviations: SD = Standard Deviation, Min = Minimum, Max = Maximum, VCI = Verbal Comprehension Index, PRI = Perceptual Reasoning Index, WMI = Working Memory Index, PSI = Processing Speed Index, FSIQ = Full Scale Intelligence Quotient, GAC = Global Adaptive Composite.

Hearing Loss based on worse ear Chang 2b. Neurocognitive scores captured by performance on the Wechsler Intelligence Scales and adaptive scores captured by parent report on the Adaptive Behavior Assessment System. All scores have a mean of 100 and standard deviation of 15. Higher scores indicate better performance or increased parent-reported adaptive skills. Group comparisons based on independent *t*-tests.

TABLE 4

Sensorineural hearing loss and cognitive functioning

Neurocognitive Measure	Effect	Estimate	SE	p value
Verbal Comprehension Index (n = 36) R ² = 0.35	Intercept	72.59	8.92	0.000
	Age at diagnosis (years)	1.28	0.62	0.048
	Sex ^a	6.26	5.62	0.274
	Maternal Education ^b	3.49	2.60	0.189
	Hearing Loss ^c	-7.41	4.46	0.107
Perceptual Reasoning Index (n = 36) R ² = 0.44	Intercept	76.50	8.37	0.000
	Age at diagnosis (years)	1.39	0.69	0.051
	Sex ^a	8.82	5.29	0.105
	Stem Cell Transplant	6.06	5.06	0.240
	Hearing Loss ^c	-11.14	4.37	0.016
Working Memory Index (n = 36) R ² = 0.43	Intercept	58.70	8.46	0.000
	Age at diagnosis (years)	1.40	0.62	0.031
	Sex ^a	18.55	5.37	0.002
	Hearing Loss ^c	-5.50	4.44	0.225
Processing Speed Index (n = 36) R ² = 0.26	Intercept	82.69	4.86	0.000
	Age at diagnosis (years)	0.47	0.54	0.386
	Posterior Fossa Syndrome	-10.27	3.76	0.010
	Hearing Loss ^c	-5.73	3.76	0.138
Full Scale Intelligence Quotient (n = 36) R ² = 0.49	Intercept	64.145	7.464	0.000
	Age at diagnosis (years)	1.567	0.549	0.007
	Sex ^a	13.812	4.741	0.006
	Hearing Loss ^c	-9.659	3.919	0.019

Note. Abbreviations: SE = standard error, cGy = centigray. Neurocognitive scores captured by performance on the Wechsler Intelligence Scales. Multivariable models were built upon a base model including age at diagnosis and presence or absence of SNHL. Additional candidate predictors were then added to each model if $p < 0.05$ in univariate analyses. For categorical predictors, absence of the condition was used as the reference group.

^a Male used as the reference level.

^b Maternal education split into three levels: no college, some college, 4-year degree or more.

^c Hearing Loss based on worse ear Chang 2b.

TABLE 5

Sensorineural hearing loss and adaptive functioning

Adaptive Measure	Effect	Estimate	SE	p value
Adaptive Conceptual Composite R ² = 0.20	Intercept	77.79	8.56	0.000
	Age at diagnosis (years)	0.63	0.63	0.323
	Sex ^a	9.21	5.44	0.100
	Hearing Loss ^b	-6.26	4.50	0.173
Adaptive Social Composite R ² = 0.07	Intercept	88.53	5.74	0.000
	Age at diagnosis (years)	0.80	0.65	0.226
	Hearing Loss ^b	-3.89	4.57	0.400
Adaptive Practical Composite R ² = 0.02	Intercept	89.78	6.65	0.000
	Age at diagnosis (years)	0.31	0.76	0.680
	Hearing Loss ^b	-4.01	5.29	0.454
Global Adaptive Composite R ² = 0.08	Intercept	87.98	6.10	0.000
	Age at diagnosis (years)	0.68	0.69	0.334
	Hearing Loss ^b	-6.24	4.85	0.207

Note. Abbreviations: SE = standard error, cGy = centigray. Adaptive scores captured by parent report on the Adaptive Behavior Assessment System. Multivariable models were built upon a base model including age at diagnosis and presence or absence of SNHL. Additional candidate predictors were then added to each model if $p < 0.05$ in univariate analyses. For categorical predictors, absence of the condition was used as the reference group.

^a Male used as the reference level.

^b Hearing Loss based on worse ear Chang 2b.