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Neurocognitive Functioning in Pediatric Craniopharyngioma: Performance before Treatment with Proton Therapy

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Abstract

The goal of this study was to investigate the impact of patient-, disease-, and treatment-related variables upon neurocognitive outcomes in pediatric patients with craniopharyngioma prior to treatment with proton therapy or observation after radical resection. For all participants (N=104), relevant clinical and demographic variables were attained and neurocognitive evaluations completed prior to irradiation or planned observation. One-sample t-tests were conducted to compare performance to published normative data. Linear models were used to investigate predictors of performance on measures where performance was below normative expectations. Participants showed poorer performance in comparison to the normative group across neurocognitive domains including executive functions (e.g., working memory; Wechsler Digit Span Backward $p=0.03$), learning and memory (e.g., California Verbal Learning Test [CVLT] Total T $p=0.00$), and fine-motor coordination (e.g., Grooved Pegboard Dominant Hand $p=0.00$). Poor performance across areas was predicted by presurgical hypothalamic involvement (e.g., Behavior Rating Inventory of Executive Function Working Memory Index Grade 2 $\beta=-7.68$, $p=0.03$; CVLT Total T Grade 2 $\beta=7.94$, $p=0.04$; Grade 3 $\beta=-9.80$, $p=0.00$), extent of surgery (e.g., CVLT Total T Resection $\beta=-7.77$, $p=0.04$; Grooved Pegboard Dominant Hand $\beta=-1.58$, $p=0.04$), and vision status (e.g., CVLT Total T Reduced vision without impairment $\beta=-10.01$, $p=0.02$; Grooved Pegboard Dominant Hand Bilateral field defect $\beta=-1.45$, $p=0.01$; Reduced vision without impairment $\beta=-2.30$, $p=0.00$). This study demonstrated that patients with craniopharyngioma show weaker neurocognitive performance in comparison to the normative population resulting from tumor, events leading to diagnosis, and early surgical intervention. Systematic investigation of neurocognitive performance before treatment with radiation therapy is

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essential to evaluating the potential risks and benefits of newer methods of radiation therapy including proton therapy.

Keywords

craniopharyngioma; cognitive outcomes; proton therapy; learning and memory

Introduction

Craniopharyngioma is a low-grade intracranial tumor arising in the sellar/suprasellar region [1]. Though craniopharyngioma is rare, between 30% and 50% are diagnosed during childhood with peak onset between 5 and 14 years of age [1,2]. Despite its benign histopathology, craniopharyngioma often results in endocrinopathies and visual disturbance secondary to the impact of tumor on the hypothalamus/pituitary axis and optic pathways, respectively [1–3].

Contemporary research suggests craniopharyngioma should be managed initially using surgery with the goal of relieving increased intracranial pressure, improving visual dysfunction, and reducing target volume for radiation therapy [3]. Given the association between pre- and postoperative hypothalamic involvement (HI) and greater morbidity, utilization of HI grading systems prior to surgical intervention and hypothalamus-sparing surgical approaches are being used. Treatment with radiation therapy following surgical resection has been recommended in contemporary studies, which have revealed comparable 5- and 10-year progression-free survival rates whether patients were treated with radical resection versus partial resection combined with radiation therapy [3]. A number of studies have recommended treatment with proton therapy (PT) given its potential to spare healthy brain tissue and improve functional and quality of life outcomes [1,3].

While the negative effects of endocrinopathies and visual dysfunction upon psychosocial adjustment and quality of life have been appreciated, the adverse impact of neurocognitive sequelae upon quality of life has recently been investigated [4]. Though pediatric patients with craniopharyngioma typically show intact intellectual functioning, deficits have been noted with sustained attention [2,5,6], processing speed [5,7,8], and learning/memory [2,5,9,10]. Poorer performance in these areas has been associated with HI [2,5], hydrocephalus, cerebrospinal fluid (CSF) diversion, younger age at the time of conventional irradiation using photons [11] and use of conventional radiation therapy generally [6]. However, the majority of studies are limited by small sample sizes and use of mixed clinical groups. Additionally, few examine predictors of poor neurocognitive outcomes.

The goal of this study was to investigate the impact of patient-, disease-, and treatment-related variables upon neurocognitive outcomes in pediatric patients with craniopharyngioma enrolled on a prospective phase II trial of limited surgery with PT and observation after radical resection. Systematic investigation of these variables before treatment is essential to evaluating potential risks and benefits of PT compared to other types of radiation therapy or comparing irradiated patients to non-irradiated patients. It was hypothesized that participants with a greater degree of preoperative HI and more extensive

surgical intervention would show poorer neurocognitive performance prior to treatment with PT or planned observation after radical surgery.

Materials and Methods

Participants

From August 2011 to May 2016 patients (N=110) were enrolled on a phase II trial of limited surgery and PT for craniopharyngioma and observation after radical resection. Participants were pediatric patients, infants through 21 years of age, newly diagnosed with craniopharyngioma by histology, cytology or neuroimaging. Patients with history of treatment with fractionated radiation therapy, intracystic P-32, intracystic bleomycin, or radiosurgery, and those who were pregnant were excluded from enrollment. Those with limited English proficiency or premorbid neurological (e.g., traumatic brain injury) or neurodevelopmental (e.g., Down syndrome, autism spectrum disorder) conditions did not receive protocol-based, cognitive evaluations. This study was approved by the Institutional Review Board, and informed consent was obtained prior to participation (RT2CR; NCT01419067). Procedure

Some patients were selected for radical surgery based upon assessment of the neurosurgeon. Participants who received less than gross total resection or no surgical resection were treated with passively-scattered proton therapy. The total cumulative dose was 54CGE using daily fractions of 1.8CGE and a 5mm clinical target volume.

Relevant demographic and clinical variables were extracted from the study database and medical charts including gender and number of surgeries (Table 1). Extent of preoperative HI was categorized as having no HI (grade 1), anterior HI (grade 2), and anterior as well as posterior HI including the mammillary bodies (grade 3) [1,2]. This categorization was based on preoperative neuroimaging after symptom onset. Extent of surgery was categorized as no surgery, placement of a catheter, or resection. CSF diversion procedures included ventriculoperitoneal (VP) shunting and endoscopic third ventriculostomy (ETV). Diabetes insipidus (DI) was categorized as present or not based on whether the patient was permanently placed on desmopressin prior to baseline cognitive assessment. Vision status with regard to visual fields was categorized as intact bilaterally or having the presence of a unilateral or bilateral field defect. Visual acuity was classified as having reduced vision either unilaterally or bilaterally with no functional impairments. Those with reduced vision with functional impairments were classified as having unilateral or bilateral involvement including unilateral blindness. Participants were also classified as having bilateral blindness. Vision status was described as not evaluable if fields or acuity could not be assessed in both eyes for reasons such as age, behavioral difficulties and blindness.

Measures

Baseline cognitive evaluations were conducted prior to initiation of PT. Intellectual ability was estimated through use of age-appropriate Wechsler scales (Table 2). These scales were normed on large, representative samples and have adequate reliability and validity [12–14].

Measures of attention (Wechsler Digit Span Forward, Conners' Continuous Performance Test-II [CPT-II]) [12–15], executive function (Wechsler Digit Span Backward and Working Memory Index [WMI], Delis-Kaplan Executive Function System [D-KEFS], Woodcock-Johnson Tests of Cognitive Abilities, 3rd Edition [WJ-III Cog], Behavior Rating Inventory of Executive Function [BRIEF] Parent Form) [12, 16–18], and memory (age-appropriate version of the California Verbal Learning Test [CVLT], Memory for Designs from the Developmental Neuropsychological Assessment, 2nd Edition for ages 3 through 16 or Designs from the Wechsler Memory Scale, 4th Edition for those over the age of 17; Table 2) [19–22] were collected. Each of these measures was normed on large, representative samples and has acceptable reliability and validity [12–22].

Measures of visuospatial processing (Beery-Buktenica Developmental Test of Visual-motor Integration, 6th Edition [Beery VMI], Beery VMI Developmental Test of Visual Perception, 6th Edition, Grooved Pegboard) [23,24], adaptive functioning (Adaptive Behavior Assessment System for Children, 2nd Edition [ABAS-II] Parent Form) [25] as well as psychosocial functioning (Behavior Assessment System for Children, 2nd Edition [BASC-2] Parent Rating Scale) [26] and academics (Woodcock-Johnson Tests of Achievement, 3rd Edition [WJ-III Ach]; Table 2) [27] were also collected. These measures were normed on large, representative samples and have adequate reliability and validity [23–27].

Statistics

Qualitative analyses were performed to characterize the sample with regard to demographic and clinical factors. One-sample t-tests (2 way; $\alpha=0.05$) were conducted to compare baseline performance among participants to the normative mean. The results were shown as average $\pm$ 1 standard deviation based upon age-standardized scores such that standard scores between 85 and 115, scaled scores between 7 and 13, t-scores between 40 and 50, and z-scores between –1.00 and 1.00 were considered average. Linear models were fitted to investigate predictors of performance on measures where participant performance was below normative expectations.

Results

Among the 110 patients originally enrolled on this study, 3 did not speak English, and 1 was unable to complete measures based upon age and sensory limitations. There were 2 patients who did not receive neurocognitive assessment until after PT. On average, participants (N=104) were approximately 10 months from diagnosis (M=0.85; SD=1.33; range=0.03–9.77) and 10 years of age at the time of participation (Table 1). The majority of the sample was between 7 and 16 years of age (64%; 0–6 years=28%, 7–16 years=64%, 17 years=8%). They were balanced by gender (48% male), but primarily Caucasian (65%). The median number of surgeries was 1 (range=0–8). The majority was categorized as having grade 3 preoperative HI (55%) at baseline, underwent surgical resection (72%), and had DI (53%). A smaller portion of the sample had CSF diversion (33%) including VP shunting and ETV. The majority of the sample had intact visual fields (64%) and no visual acuity deficits (73%).

T-tests revealed average global intelligence (Wechsler Full Scale Intelligence Quotient) with stronger nonverbal reasoning than expected (Wechsler Perceptual Reasoning Index; Table 2). Attention was consistent with normative expectations (Wechsler Digit Span Forward; CPT-II Omissions, Hit Response Time, Detectability, Response Style) or above normative expectations (CPT-II Commissions; BASC-2 Attention Problems). Aspects of executive functioning were intact (D-KEFS Color-word Interference, BRIEF Global Executive Composite, Behavioral Regulation Index, Metacognition Index); however, performance on tasks of working memory was weaker in comparison to the normative group (Wechsler Digit Span Backward; BRIEF WMI). There was also difficulty with verbal fluency (WJ-III Cog Retrieval Fluency). Verbal learning and memory (CVLT Total Trials; Short and Long Delay Free and Cued Recall) as well as visual memory (immediate visual memory) were below normative expectations.

Though fine-motor coordination was problematic (Grooved Pegboard Dominant and Nondominant Hand), visual discrimination and visuomotor integration were consistent with expectations (Beery VMI; Table 2). Adaptive functioning was intact (ABAS-II Global Adaptive Composite, Conceptual, Social) with the exception of practical adaptive skills (e.g., independent navigation of the home/community, observation of rules related to health/safety, completion of self-care tasks). Fewer externalizing behaviors (e.g., aggression, hyperactivity) than expected were found (BASC-2 Externalizing Problems); however, greater internalizing behaviors (e.g., anxiety, depression) were noted (Internalizing Problems). Basic reading (WJ-III Ach Letter-word Identification) and arithmetic (Calculation) were intact; however, speeded reading (Reading Fluency) and mathematics (Math Fluency) were below expectations.

Linear models analysis suggested that comparatively reduced working memory and verbal fluency were predicted by presurgical HI (Table 3). More specifically, grade 1 HI was predictive of poorer working memory in the naturalistic setting (BRIEF WMI) in comparison to grade 2; however, participants with grades 1 and 3 HI performed similarly. In contrast, grade 3 HI was predictive of decreased verbal fluency (WJ-III Cog Retrieval Fluency) in comparison to grade 2 HI with participants with grade 1 and 2 HI performing similarly. Poorer performance in learning/memory was predicted by preoperative HI, extent of surgery and vision status. For presurgical HI, participants with grades 1 and 3 HI performed more poorly than participants with grade 2 HI (CVLT Total T, Short Delay Free Recall, Long Delay Free and Cued Recall). Participants with grade 3 HI performed more poorly than those with grade 2 HI for Short Delay Cued Recall. In terms of extent of surgery, participants who underwent resection performed more poorly than those who had received a catheter (CVLT Total T, Long Delay Free Recall). With regard to vision status, participants with reduced vision without impairment performed more poorly than those without acuity deficits (CVLT Total T, Short and Long Delay Free and Cued Recall), and those with bilateral visual field defects performed more poorly than those without field defects (immediate visual memory).

Limited fine-motor dexterity was predicted by age at baseline evaluation such that older participants performed more poorly (Grooved Pegboard Dominant Hand), number of surgeries such that those with a higher number of surgeries performed more poorly

(Dominant and Nondominant Hands), extent of surgery, and vision status (Table 3). With regard to extent of surgery, worse fine-motor performance with the dominant hand was predicted by resection in comparison to catheter. Weaker fine-motor performance with the nondominant hand was associated with resection in comparison to participants without surgery. In terms of vision status, worse fine-motor performance with the dominant hand was predicted by bilateral field defects and reduced visual acuity without functional impairments in comparison to participants with no acuity deficits or field defects, respectively; poorer fine-motor functioning of the nondominant hand was related to unilateral and bilateral field defects in comparison to those with no field defects. Finally, worse practical adaptive functioning (ABAS-II Practical) and greater mood disruption (BASC-2 Internalizing Problems) were predicted by DI and vision status. More specifically, participants with bilateral blindness showed greater trouble with adaptive skills than those without acuity deficits; and, participants with unilateral visual field defects showed fewer internalizing symptoms than those without field defects.

Discussion

This study demonstrated that patients with craniopharyngioma show weaker neurocognitive performance in comparison to the normative population prior to treatment with PT or observation after radical resection. More specifically, poorer performance in aspects of executive functions, learning/memory, motor abilities, adaptive skills, psychosocial adjustment, and academic skills were found. With the exception of academic skills, baseline performance below normative expectations in each of these areas was predicted by specific clinical variables. Knowledge of pre-radiation therapy cognitive performance, and clinical risk factors, is crucial to evaluating risks involved with radiation therapy, particularly as new radiation therapy approaches (e.g., PT) are increasing in use.

Participants showed reduced performance with regard to executive functions including working memory in the naturalistic setting and verbal fluency prior to radiation therapy. Though functioning in this domain has been consistent with normative expectations in other studies [2,7,8,28], these studies were limited by small sample sizes. Consistent with previous studies, weaker performance was found in verbal and visuospatial learning and memory [2,5,7,9,10]. This was the case across components of verbal memory (e.g., short and long term, free and cued). While short-term visuospatial memory was comparatively worse, long-term visuospatial memory was intact. This pattern of performance is not altogether consistent with previous studies [9,10], but may suggest that visuospatial, as opposed to verbal, information was better consolidated over time. This may also be related to differences in the nature of the visual memory task (e.g., recognition-based, comparatively structured). Difficulty with fine-motor coordination bilaterally, practical adaptive skills, internalizing problems, and academic fluency were found, but have not been investigated in previous studies aimed at pediatric patients with craniopharyngioma thus adding meaningfully to the existing literature.

Intelligence at baseline was intact, which is consistent with previous research [2,4–11]. In contrast, attention and nonverbal reasoning that are stronger than expectations is not typically found [2,4–6]; however, several studies have found adequate attention on objective

measures [7,8,28]. Studies that found difficulty with attention [2,5,6] are limited by small sample sizes and use of mixed clinical groups. The strong performance among the sample on tasks of nonverbal reasoning may be related to fewer participants completing these measures (e.g., those with substantial visual impairments); but, the number of patients who completed measures of verbal and nonverbal reasoning did not differ greatly.

Performance below normative expectations in various neurocognitive domains was predicted by presurgical HI, number and extent of surgeries, and vision status. Difficulties with executive functioning in the areas of verbal fluency and working memory in the naturalistic setting were associated with HI. Though working memory performance on lab-based tasks or objective measures of working memory was below normative expectations, difficulty here was not predicted by presurgical HI. While the impact of HI upon neurocognitive functions has been shown in previous studies, the patterns of association across degrees of HI in this study were not fully consistent with hypotheses [2,5]. More specifically, participants with the highest degree of HI showed the most difficulty with verbal fluency, which was consistent with hypotheses; but, those with involvement of the anterior hypothalamus (grade 2 HI) showed stronger working memory performance in their naturalistic settings in comparison to those without HI (grade 1) and with the highest degree of HI (grade 3). This pattern of performance also emerged on measures tapping verbal learning/memory. Though comparative difficulty in this domain was not surprising given the sellar/suprasellar location of craniopharyngioma and associated potential for disruption of Papez circuit and diencephalic-hippocampal circuitry, the tendency for grade 2 HI to be associated with the strongest performance may be related to the small sample size associated with grade 1 HI. Stronger performance among those with grade 1 involvement could become more apparent with a larger sample size. It is also possible that participants with grade 2 HI differed systematically from those with grades 1 and 3 HI in terms of a third variable (e.g., income, parent education level) that played a protective role in cognitive functioning.

Weaker performance in learning/memory was also predicted by surgical intervention, which is again consistent with disruption of memory circuitry. In line with hypotheses, greater extent of surgical intervention (e.g., resection versus catheter) was associated with poorer verbal memory. Fine-motor difficulties bilaterally were also associated with greater extent of surgical intervention. Additionally, fine-motor deficits increased as the number of surgical interventions increased. Given the midline location of craniopharyngioma, it is possible that disruption of basal ganglia occurred during surgical intervention resulting in relative fine-motor difficulty. Finally, poorer fine-motor performance was associated with age at baseline such that participants assessed at an older age showed poorer performance. This may be related to normative properties of the measure used given that normative expectations allow for smaller discrepancies with older age and more refined motor systems.

Vision status was associated with poorer performance in fine-motor dexterity, adaptive skills and learning/memory. Reduced fine-motor control bilaterally was related to unilateral and bilateral visual field defects as well as reduced visual acuity without functional impairment. Visual dysfunction was likely the result of involvement of the optic chiasm given its proximity to the sellar/suprasellar region. The relationship between DI as well as bilateral blindness and practical adaptive functioning is likely related to trouble independently

engaging in self-care tasks (e.g., toileting) and navigating the home and surrounding community. DI also increases medical management (e.g., monitoring fluid intake and voiding) potentially resulting in greater dependence on caregivers. Similarly, the association between parent-reported concerns with internalizing symptoms and DI may be the result of difficulty with participants' psychosocial adjustment to this condition. Participants with reduced visual acuity without functional impairments and those with bilateral field defects experienced greater difficulty with verbal learning/memory and visuospatial memory, respectively. This may be related to greater difficulty utilizing visualization strategies to aid in memory tasks, but further research is warranted.

This study characterized neurocognitive functioning of a large group of patients with craniopharyngioma at baseline, which has not previously occurred in the literature. Ultimately, this allows for better comparison of risks and benefits of PT to other radiation therapy techniques in terms of preservation of neurocognitive functions. This study also examined predictors of performance below normative expectations across neurocognitive domains, which can inform treatment planning and intervention. This suggests the need to reduce the extent of surgery or number of surgeries in certain situations. However, there are limitations associated with this study. It is important to investigate changes across neurocognitive domains following treatment with PT. Studies of this nature are currently underway. It will be helpful to compare the performance of patients treated with PT to a well-matched cohort treated with techniques like photon radiation therapy. Investigation of the impact of additional clinical factors such as sleep and aerobic fitness and psychosocial factors like income and parent education level on neurocognitive outcomes will be useful in informing treatment for this population.

Conclusion

Patients with craniopharyngioma show neurocognitive performance that is significantly weaker than the normative group at the time of diagnosis and prior to adjuvant therapy or observation. Poorer performance is predicted by clinical variables, which can be used to inform treatment and intervention planning. Accurate characterization of the neurocognitive functioning of this population at baseline sets the stage for more precisely comparing different methods of radiation therapy for potential preservation of neurocognitive functions.

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Table 1

Demographic and Clinical Variables

	<i>M ± SD</i>	Range	n (%)
Age at participation	9.84 ± 4.74	0–21	
Gender (male)			50 (48.08)
Race			
Caucasian			68 (65.40)
African American			16 (15.40)
Asian			4 (3.80)
Other ^a			16 (15.40)
HI ^b			
Grade 1			18 (17.30)
Grade 2			28 (26.90)
Grade 3			58 (55.80)
Number of surgeries (median)	1.00	0–8	
Extent of surgery			
None			12 (11.54)
Catheter			17 (16.35)
Resection			75 (72.12)
CSF diversion ^c (present)			34 (32.69)
DI ^d (present)			55 (52.88)
Vision status			
Visual fields			
Intact bilaterally			67 (64.40)
Unilateral field defect			7 (6.70)
Bilateral field defect			22 (21.20)
Unassessable ^e			8 (7.70)
Visual acuity			
No deficits			76 (73.10)
Reduced vision, no impairment ^f			10 (9.60)
Reduced vision, impairment ^f			
Unilateral ^g			6 (5.80)
Bilateral ^g			10 (9.60)
Blind ^h			1 (0.96)
Unassessable ^e			1 (0.96)

HI=hypothalamic involvement; CSF=cerebrospinal fluid; DI=diabetes insipidus

^aOther race was composed of participants with race marked as “Unknown”

^bGrade 1=no HI; Grade 2=anterior HI; Grade 3=anterior and posterior HI including mammillary bodies

^cIncludes ventriculoperitoneal shunting and endoscopic third ventriculostomy

^d Determined based on whether patient was prescribed desmopressin prior to baseline cognitive evaluation

^e As a result of age, behavioral difficulties, and blindness

^f Reduced vision unilaterally and bilaterally

^g Includes unilateral blindness

^h Bilaterally

Table 2**Baseline Cognitive Performance**

	<i>M ± SD</i>	<i>p</i>
Wechsler		
Full Scale Intelligence Quotient (SS; n=93)	100.75 ± 16.02	0.65
Verbal Comprehension Index (SS; n=80)	99.83 ± 16.73	0.93
Perceptual Reasoning Index (SS; n=78)	104.90 ± 17.92	0.02 *
Working Memory Index (SS; n=81)	95.99 ± 15.25	0.02 *
Digit Span (ScS; n=81)	9.30 ± 2.93	0.03 *
Digit Span Forward (ScS; n=76)	9.62 ± 3.09	0.28
Digit Span Backward (ScS; n=76)	9.24 ± 3.00	0.03 *
Processing Speed Index (SS; n=83)	98.08 ± 17.70	0.33
CPT-II		
Omissions (T; n=67)	52.42 ± 14.39	0.17
Commissions (T; n=67)	46.76 ± 10.10	0.01 *
Hit Response Time (T; n=67)	51.09 ± 11.46	0.44
Detectability (T; n=67)	48.29 ± 9.04	0.13
Response Style (T; n=67)	51.45 ± 10.92	0.28
D-KEFS		
CWI Inhibition Completion (ScS; n=52)	10.60 ± 3.30	0.20
CWI Inhibition Total Errors (ScS; n=50)	9.72 ± 2.63	0.46
CWI Inhibition/Switching Completion (ScS; n=50)	10.08 ± 3.34	0.87
CWI Inhibition/Switching Total Errors (ScS; n=49)	9.35 ± 3.01	0.14
WJ-III Cog Retrieval Fluency (SS; n=87)	94.97 ± 15.82	0.00 **
BRIEF		
Global Executive Composite (T; n=97)	50.38 ± 11.47	0.74
Behavioral Regulation Index (T; n=79)	50.24 ± 10.88	0.85
Metacognition Index (T; n=78)	49.44 ± 10.77	0.65
Working Memory Index (T; n=98)	52.55 ± 11.69	0.03 *
CVLT		
Total Trials (T; n=73)	44.32 ± 11.63	0.00 **
Short Delay Free Recall (Z; n=73)	-0.43 ± 1.19	0.00 **
Short Delay Cued Recall (Z; n=72)	-0.38 ± 1.19	0.01 *
Long Delay Free Recall (Z; n=73)	-0.48 ± 1.23	0.00 **
Long Delay Cued Recall (Z; n=72)	-0.46 ± 1.22	0.00 **
Immediate visual memory (ScS; n=66) ^a	8.99 ± 3.40	0.02 *
Delayed visual memory (ScS; n=64) ^b	9.34 ± 3.42	0.13
Beery VMI (SS; n=92)	98.37 ± 12.23	0.20
Visual Perception (SS; n=89)	98.32 ± 15.94	0.32
Grooved Pegboard		

	<i>M ± SD</i>	<i>p</i>
Dominant Hand (Z; n=78)	-0.67 ± 2.08	0.01 *
Nondominant Hand (Z; n=74)	-0.44 ± 1.72	0.03 *
ABAS-II		
Global Adaptive Composite (SS; n=95)	97.53 ± 16.08	0.14
Conceptual (SS; n=98)	99.13 ± 15.15	0.57
Social (SS; n=99)	101.22 ± 15.35	0.43
Practical (SS; n=96)	95.16 ± 17.54	0.01 *
BASC-2		
Externalizing Problems (T; n=98)	44.91 ± 9.49	0.00 **
Internalizing Problems (T; n=97)	54.36 ± 12.83	0.00 **
Behavioral Symptoms Index (T; n=98)	48.27 ± 10.48	0.10
Attention Problems (T; n=98)	45.77 ± 10.78	0.01 *
WJ-III Ach		
Letter-word Identification (SS; n=76)	101.42 ± 14.19	0.39
Reading Fluency (SS; n=70)	96.54 ± 14.06	0.04 *
Calculation (SS; n=74)	97.51 ± 18.36	0.25
Math Fluency (SS; n=72)	91.89 ± 16.78	0.00 **

CPT-II=Conners' Continuous Performance Test-II; D-KEFS=Delis-Kaplan Executive Function System; CWI=Color-word Interference; WJ-III Cog=Woodcock-Johnson Tests of Cognitive Abilities, 3rd Edition; BRIEF=Behavior Rating Inventory of Executive Function; CVLT=California Verbal Learning Test; Beery VMI=Beery-Buktenica Developmental Test of Visual-motor Integration, 6th Edition; ABAS-II=Adaptive Behavior Assessment System, 2nd Edition; BASC-2=Behavior Assessment System for Children, 2nd Edition; WJ-III Ach=Woodcock-Johnson Tests of Achievement, 3rd Edition

SS=standard score ($M=100$; $SD=15$); ScS=scaled score ($M=10$; $SD=3$); T=t-score ($M=50$; $SD=10$); Z=z-score ($M=1.00$; $SD=0.05$)

^aRepresents combined scores from Developmental Neuropsychological Assessment, 2nd Edition (NEPSY-II) Memory for Designs Total and Wechsler Memory Scale, 4th Edition (WMS-IV) Designs I

^bRepresents combined scores from the NEPSY-II Memory for Designs Delayed Total and WMS-IV Designs II one-sample t-test

*
 $p < 0.05$

**
 $p < 0.01$

Table 3**Predictors of Poor Performance by Cognitive Domain**

	Category	β	p
Executive functions			
Preoperative HI			
BRIEF Working Memory Index	Grade 1 vs. Grade 2	-7.68	0.04 *
WJ-III Cog Retrieval Fluency	Grade 3 vs. Grade 2	-9.91	0.02 *
Learning and memory			
Preoperative HI			
CVLT Total T	Grade 2 vs. Grade 1	7.95	0.05 *
	Grade 3 vs. Grade 2	-9.80	0.00 **
CVLT Short Delay Free Recall	Grade vs. Grade 1	1.05	0.00 **
	Grade 3 vs. Grade 2	-1.18	<0.00 **
CVLT Short Delay Cued Recall	Grade 3 vs. Grade 2	-1.03	0.00 **
CVLT Long Delay Free Recall	Grade 2 vs. Grade 1	0.99	0.01 *
	Grade 3 vs. Grade 2	-1.10	0.00 **
CVLT Long Delay Cued Recall	Grade 2 vs. Grade 1	1.22	0.00 **
	Grade 3 vs. Grade 2	-1.24	<0.00 **
Extent of resection			
CVLT Total T	Resection vs. catheter	-7.77	0.05 *
CVLT Long Delay Free Recall	Resection vs. catheter	-0.90	0.03 *
Visual fields			
Immediate visual memory	Bilateral field defect vs. defect	-2.14	0.04 *
Visual acuity			
CVLT Total T	Reduced vision, no impairment vs. no impairment	-10.01	0.02 *
CVLT Short Delay Free Recall	Reduced vision, no impairment vs. no impairment	-0.94	0.04 *
CVLT Short Delay Cued Recall	Reduced vision, no impairment vs. no impairment	-1.23	0.01 *
CVLT Long Delay Free Recall	Reduced vision, no impairment vs. no impairment	-1.16	0.01 *
CVLT Long Delay Cued Recall	Reduced vision, no impairment vs. no impairment	-1.37	0.00 **
Fine-motor dexterity			
Age at baseline evaluation			
Grooved Pegboard Dominant Hand		-0.12	0.04 *
Number of surgeries			
Grooved Pegboard Dominant Hand		-0.50	0.01 *
Grooved Pegboard Nondominant Hand		-0.54	0.00 **
Extent of resection			
Grooved Pegboard Dominant Hand	Resection vs. catheter	-1.58	0.04 *
Grooved Pegboard Nondominant Hand	No Surgery vs. resection	1.39	0.02 *

	Category	β	p
Visual fields			
Grooved Pegboard Dominant Hand	Bilateral field defect vs. no impairment	-1.46	0.01 *
Grooved Pegboard Nondominant Hand	Unilateral field defect vs. no impairment	-1.73	0.03 *
	Bilateral field defect vs. no impairment	-0.98	0.05 *
Visual acuity			
Grooved Pegboard Dominant Hand	Reduced vision, no impairment vs. no impairment	-2.30	0.00 **
Adaptive skills			
DI			
ABAS-II Practical	Yes vs. no	-8.13	0.02 *
Visual acuity			
ABAS-II Practical	Bilateral blindness vs. no impairment	-54.33	0.00 **
Psychosocial functioning			
DI			
BASC-2 Internalizing Problems	Yes vs. no	5.77	0.03 *
Visual fields			
BASC-2 Internalizing Problems	Unilateral field defect vs. no impairment	-10.99	0.02 *

HI=hypothalamic involvement; BRIEF=Behavior Rating Inventory of Executive Function; WJ-III Cog=Woodcock-Johnson Tests of Cognitive Abilities, 3rd Edition; CVLT=California Verbal Learning Test; DI=diabetes insipidus; ABAS-II=Adaptive Behavior Assessment System, 2nd Edition; BASC-2=Behavior Assessment System for Children, 2nd Edition

Linear mixed effects models

*
 $p < .05$

**
 $p < .01$