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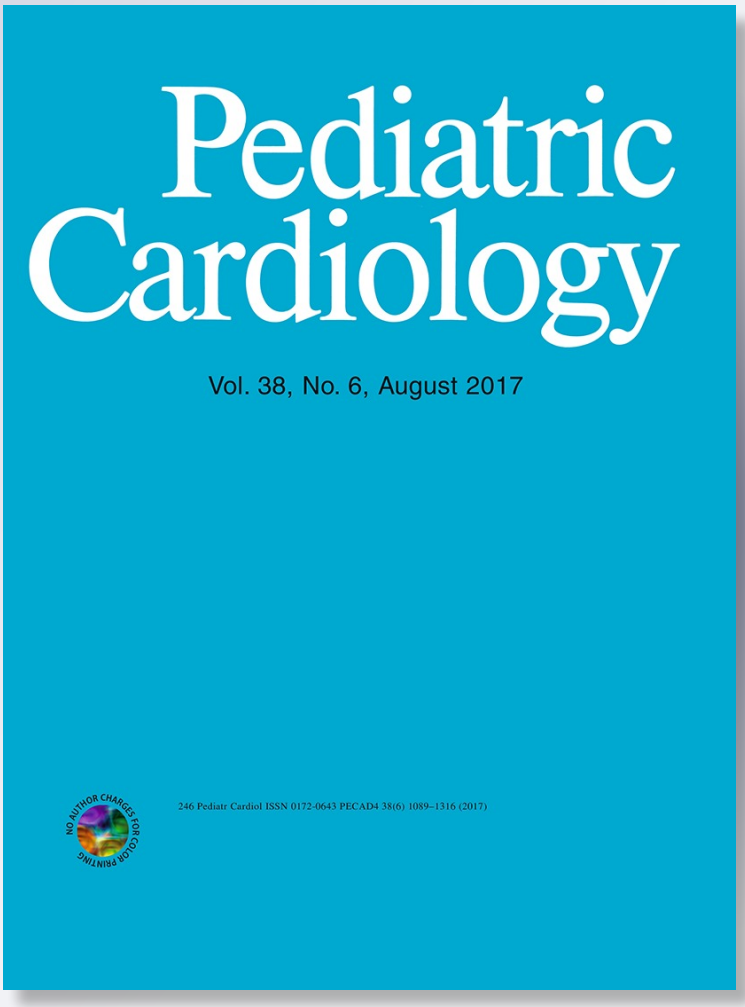

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REVIEW ARTICLE

Cognitive Development of School-Age Hypoplastic Left Heart Syndrome Survivors: A Single Center Study

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Abstract Neurological and radiologic research results show an abnormal cerebral microstructure as well as abnormal neurodevelopment in patients treated for hypoplastic left heart syndrome. The aim of this study was to assess the varying cognitive performance these children have developed in dependence upon prenatal diagnosis, surgical techniques, surgical learning effects, anatomy, perfusion techniques, gender, pedagogic, and sociodemographic parameters in comparison to age-adjusted normative values. School-age children (6.3–16.9 years) with hypoplastic left heart syndrome, who were treated at the Children's heart Center Linz between 1997 and 2009, ($n = 74$), were surveyed in reference to cognitive achievements. 43 patients were examined prospectively by psychologists using the Wechsler intelligence scale for children IV in order to determine the respective total intelligence quotient index for each child's developmental stage. The mean index was 84.5 (percentile rank 26.4). The statistical spread and standard deviation ranged from a minimum of 40 to a maximum of 134 ± 20.8. The results for verbal comprehension, perceptual reasoning, and processing speed corresponded with total index results and were thus lower than the mean value of the normative values. The assessment of working memory showed results in the average. Prenatal diagnosis, type of lung perfusion, anatomy, and various cerebral perfusion techniques did not significantly affect the cognitive results of the patients. The results show that hypoplastic left heart syndrome patients can be successfully tutored formally as well as personally in cognitive areas, although when compared to healthy children, they showed lower results for intellectual area parameters.

Keywords Hypoplastic left heart syndrome · Cognitive development · Long-term follow-up

Abbreviations

WISC	Wechsler intelligence scale for children
PRI	Perceptual reasoning index
PSI	Processing speed index
VCI	Verbal comprehension index
WMI	Working memory index
IQ-Index	Intelligence quotient index
ANOVA	Analysis of variance

Introduction

Neurodevelopmental delay has been described in children with critical congenital left heart disease. Neurological and radiological research results [1–5] show that neonates with hypoplastic left heart syndrome (HLHS) show an abnormal cerebral microstructure and their intrauterine brain growth may be delayed. Postnatal treatment of HLHS includes extensive cardiac surgery in the neonatal period using cardiopulmonary bypass often followed by long intensive-care stays with hemodynamic instabilities [6]. Later, these children have to undergo at least two further cardiac surgeries on bypass (bi-directional Glenn procedure and Fontan operation, [7–12]). Whether neurodevelopmental problems are caused primarily by prenatal or postnatal factors is still unclear. Many hypoplastic left heart

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syndrome patients have now reached school age, and there is a lack of data about their cognitive development [13–18].

Thus it was the aim of the study to determine

(1) what type of total and differentiated cognitive performance children with HLHS have developed in comparison to the normative sample of same-age healthy children,
(2) and whether the respective outcome was related to prenatal diagnosis, surgical techniques, surgical learning effects, anatomy, perfusion techniques, gender, or pedagogic, educational, and sociodemographic parameters.

Materials and Methods

From 1997 to 2009, 149 children ($n = 149$) with HLHS were admitted to the Children's Heart Center Linz. Sixty-four patients died before entering school. Of these, 25 newborns died before surgical treatment due to circulatory collapse or because the parent(s) chose comfort care. All other patients ($n = 124$) underwent a Norwood stage I operation in the newborn period, a bi-directional Glenn procedure at the age of 3–4 months, and a Fontan operation around the age of 3 years, all at our institution. Another 39 children (31%) died before entering school; 24 died between stages 1 and 2; 14 children died after a bi-directional Glenn procedure between stages 2 and 3, and one child died after a Fontan operation. Of the remaining 85 patients, the following 42 patients did not participate in the study: 30 children whose parents denied informed consent; one boy with severe hypoxic encephalopathy following a Fontan operation; and 11 children from non-German-speaking foreign countries. Thus, 43 patients (mean age 10.3 ± 3.1 years; range 6.3–16.9 years) underwent complete testing and the survey (Fig. 1), ([19], unpublished data in our institution). There were no patients included who were tested and died thereafter.

Twenty-one children had been diagnosed prenatally; 28 were male; 33 had received a Sano-shunt at the time of the Norwood operation and ten had a modified Blalock–Taussig shunt; 28 patients had aortic atresia; 15 had aortic stenosis; five were operated in deep hypothermic circulatory arrest; nine patients were operated using antegrade cerebral perfusion, and 28 patients underwent double perfusion technique [1].

The results were compared to the mean variation of the age-adjusted normative values [20].

There were no data in the investigated group concerning morphological changes of the brain, no sonographic or MRI examinations which could be related to the results. HLHS patients who participated in the study attended the following school types: Primary school ($n = 22$), secondary school ($n = 8$), academic secondary school ($n = 2$), special needs school ($n = 4$), secondary school with a business emphasis ($n = 2$), apprenticeship ($n = 1$), Montessori or Freinet school ($n = 2$), unemployed after compulsory schooling ($n = 2$).

Three patients were diagnosed with attention-deficit hyperactivity disorder, two with protein-losing enteropathy, eight with sensorimotor disorders (such as problems with coordination of sensory and motor signals while writing, holding crayons spatial orientation deficits.), and two with seizures and one with autism.

This study was approved by the local IRB (ID-number J16-01).

On the basis of Wechsler intelligence scale for children IV, the particular total intelligence quotient index for the developmental stage of each child, differentiated by the indices for verbal comprehension, perceptual reasoning, working memory, and processing speed, was surveyed [20].

The verbal comprehension index assesses linguistic concept formation, linguistic deductive reasoning, and acquired knowledge.

The perceptual reasoning index consists of sub-tests which measure perceptual organization and logical reasoning; in particular, fluid logical thinking was charted.

The working memory index assesses attention, concentration, and working memory, and the processing speed index charts the speed of mental and graphomotor processing.

By means of semi-standardized questioning as a way of performing qualitative content analysis [21], social skills and teacher–student relationships were assessed.

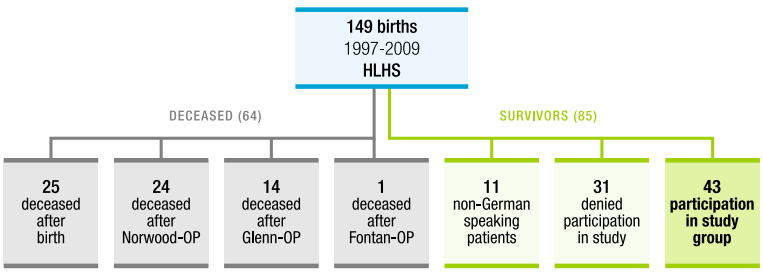

Fig. 1 Sample, HLHS 1997–2009

The psychological surveys were combined with check-up appointments and took place between November 2014 and April 2015.

Statistical Analysis

The data are presented as mean ± standard deviation. Independent-samples *t* test and analysis of variance were used for group comparisons. *p*-values < 0.05 were considered statistically significant. Due to small group size, the *p*-values from the equivalent non-parametric tests (Mann–Whitney *U* test and Kruskal–Wallis test) are also reported (second *p*-value). For significant group differences, effect size estimates (Cohen's d) are reported. In addition, effect size estimates are also reported from case to case for statistically non-significant results, which might be of surgical importance [22]. The statistical analyses were performed using the statistical software SPSS 22.0 for Windows.

Results

All 43 children reached an average intelligence quotient index of 84.5 (percentile rank 26.4) with a standard deviation of 20.8. The spread ranged from a minimum value of 40 to a maximum value of 134. The results of the respective subindices can be seen in Table 1. In verbal comprehension, perceptual reasoning, and processing speed, the values corresponded to the total index results. For working memory, the results were within average.

Table 2 shows the results of the HLHS group compared to the mean variation of the normative values. While HLHS patients were strong in the "below average" and "far below average" ranges and weak in the "average" and "above average" ranges, HLHS patients were strong in the "far above average" range with 4.6% (2/43 patients). There was no significant difference between pre- and peripubertal patients in comparison.

Only for the "working memory" index did the results of the HLHS patients correspond to the distribution (see Table 3).

Prenatal Diagnosis

Twenty-one patients had been given a prenatal diagnosis and 22 were diagnosed after birth. Prenatally diagnosed patients showed a higher intelligence quotient index value in the total result 86.9 ± 21.2 versus patients with unknown prenatal diagnosis (total score 82.2 ± 20.7) as well as for all subscales. However, both the total score and the subscales showed no significant difference.

HLHS—Anatomy

Fifteen patients had aortic stenosis and 28 aortic atresia. The total range and also all subindices showed a preference toward aortic stenosis, however, never to a significant degree.

Shunt Type at the Time of the Norwood Operation [23, 24]

Out of this group, the first ten newborns had a modified Blalock–Taussig shunt placed, followed by thirty-three newborns who received a Sano-shunt instead. Sano-shunt patients showed significant better results in verbal comprehension (Sano-shunt: Intelligence quotient index 87.4 ± 22.9; modified Blalock–Taussig shunt: Intelligence quotient index 72.9 ± 21.6; $p = 0.05$*, *t*-value 1.78, effect size: −0.643) and perceptual reasoning (Sano-shunt: Intelligence quotient index 86.4 ± 17.1; modified Blalock–Taussig shunt: Intelligence quotient index 74.5 ± 19; $p = 0.05$*, *t*-value 1.85, effect size: −0.68). The total score and working memory index only showed positive trends towards the patients with Sano-shunts, but no significance.

Gender

Twenty-eight children were male and 15 female. A significant difference was found in verbal comprehension, with boys showing higher ability (males: intelligence quotient index 90.5 ± 23.6; females: intelligence quotient index 72.0 ± 17.4; *t*-value: 2.65, $p = 0.017$*, effect size: −0.85). The total scales as well as the other subscales were not significantly different [25].

Table 1 Wechsler intelligence scale for children IV (WISC IV): results (IQ-Indices) of the total study group: total, verbal comprehension (VCI), perceptual reasoning (PRI), working memory (WMI), processing speed (PSI)

	n	Minimum	Maximum	Mean value	Percentile rank	Standard deviation
WISC-total	43	40.0	134.0	84.5	26.4	20.8
WISC-VCI	43	45.0	150.0	84.0	25.6	23.2
WISC-PRI	43	47.0	117.0	83.6	24.9	18.0
WISC-WMI	42	62.0	144.0	101.8	50.4	18.8
WISC-PSI	42	43.0	134.0	84.5	23.8	18.0

Distribution, mean values, percentile rank, and standard deviation for cognitive development scales

Table 2 Wechsler intelligence scale for children (WISC IV): total results as compared to the normative values

Percentile rank	WISC total (%)	*n*	IQ-index/normal distribution
0–2.2% far below average	25.5	11	(<69) 2.2%
2.2–15.8% below average	27.9	12	(70–84) 13.6%
15.8–84% average	39.4	17	(85–114) 68.2%
84–97.6% above average	2.3	1	(115–129) 13.6%
97.6–100% far above average	4.6	2	(>130) 2.2%

Table 3 Wechsler intelligence scale for children (WISC IV): working memory in comparison

Percentile rank (%)	WISC working memory (%)	*n*	IQ-index/normal distribution
0–2.2	4.8	2	(<69) 2.2%
2.2–15.8	7.2	3	(70–84) 13.6%
15.8–84	66.6	29	(85–114) 68.2%
84–97.6	14.3	6	(115–129) 13.6%
97.6–100	7.2	3	(>130) 2.2%

Learning Curve/Surgery Timeline

To assess possible effects of a learning curve, the total group under review was divided into patients operated before 2004 ($n = 14$) and after 2004 ($n = 29$). No significant differences in intellectual development could be found. According to the qualitative description by the International Classification of Diseases and Health-Related Problems 10, the results in total, verbal comprehension, and perceptual reasoning rose from below average to average after 2004 (above the index value of 85).

Perfusion Technique During Norwood Operation

Five patients from the earlier period were operated in deep hypothermic circulatory arrest; the next ten patients had an antegrade cerebral perfusion, followed by 28 patients with double perfusion technique.

The respective perfusion techniques did not significantly ($p < 0.05$) affect the cognitive results of HLHS patients; the calculated effect size measures (Cohen's d) showed several small to medium differences: Wechsler Intelligence Scale for Children total: double perfusion technique to deep hypothermic circulatory arrest ($d = 0.336$); verbal comprehension: double perfusion technique to antegrade cerebral perfusion ($d = 0.474$); perceptual reasoning: double perfusion technique to deep hypothermic circulatory arrest ($d = 0.605$); working memory: antegrade cerebral perfusion to double perfusion technique ($d = -0.401$); processing speed: antegrade cerebral perfusion to double perfusion ($d = -0.523$). The double perfusion tended to affect cognitive development more positively than deep hypothermic circulatory arrest. Patients who had been treated by antegrade cerebral perfusion showed better values for working memory and processing speed.

HLHS patients ($n = 28$) treated with double perfusion technique showed average results in all intelligence quotient index values (see Table 4, Wechsler intelligence scale for children: perfusion techniques).

School

Teacher–student relationships were evaluated by asking the parents to assess this relationship according to the grading system used in Austrian schools: excellent (1, $n = 2$); good (2, $n = 21$); satisfactory (3, $n = 12$); adequate (4, $n = 4$); unsatisfactory (5, $n = 5$). Children whose parents had rated the teacher–student relationship as excellent also showed significantly better results in the cognitive area, especially in verbal comprehension (excellent: intelligence quotient index 132.5 ± 24.7; good: intelligence quotient index 82.0 ± 23.3; satisfactory: intelligence quotient index 81.6 ± 16.2; adequate: intelligence quotient index 97.5 ± 12.6; $p = 0.028$).

Children with severe illness experienced in early childhood sometimes develop deficits in social interaction with their peers [26]. The parents' assessments of their child's social skills on a scale of 'very bad' ($n = 4$), 'marginal' ($n = 8$), 'satisfactory' ($n = 18$), 'good' ($n = 10$), and 'excellent' ($n = 3$) showed a significant difference in achievement between patients with marginal and excellent social skills compared with peers (excellent: intelligence quotient index 111.2 ± 23.0; marginal: intelligence quotient index 85.7 ± 21.9). The results of the other patients did not differ significantly ($p = 0.212$).

Parental Education

In all areas, HLHS children whose parents had a university or college degree ($n = 11$, intelligence quotient index

Table 4 Wechsler Intelligence Scale for Children (WISC IV): perfusion techniques

WISC/perfusion	Deep hypothermic circulatory arrest ($n = 5$) IQ-index M ± SD	Antegrade cerebral perfusion ($n = 10$) IQ-index M ± SD	Double perfusion technique ($n = 28$) IQ-index M ± SD	p (ANOVA)	p (Kruskal–Wallis Test)
WISC-total	79.0 ± 13.8	83.0 ± 23.9	86.0 ± 21.6	$p < 0.7$	$p < 0.768$
WISC-VCI	79.2 ± 13.6	75.6 ± 75.7	87.2 ± 23.9	$p < 0.4$	$p < 0.341$
WISC-PRI	75.8 ± 17.3	81.0 ± 22.8	86.1 ± 16.9	$p < 0.4$	$p < 0.365$
WISC-WMI	99.0 ± 7.6	108.3 ± 21.0	100.2 ± 19.9	$p < 0.5$	$p < 0.717$
WISC-PSI	87.0 ± 5.4	92.0 ± 15.1	81.7 ± 20.2	$p < 0.3$	$p < 0.065$

87.2 ± 25.2) showed better performance outcomes than children whose parents had lower levels of education (apprentice training, $n = 17$, intelligence quotient index 78.0 ± 12.4; compulsory education, $n = 3$, intelligence quotient index = 66.6 ± 37.8, $p < 0.05$).

Characteristics of Children with Above-Average Performance

Three HLHS patients showed above-average performance. Their ages were: 6.3/10.8/12.4 years, respectively; two male, one female; their total intelligence quotient index was 134/131/116, respectively; two had a prenatal diagnosis; all of them had a Sano-shunt at the time of their Norwood operation; two had a double perfusion technique during their Norwood procedure, one an antegrade cerebral perfusion; the teacher–student relationship was rated 'very good' for all; one patient went to elementary school; two attended secondary school, and their social competence was estimated 'high' by the parents; parental education: two had A-Level (university entrance exam), one had a university education.

Discussion

The results of this study show that the average cognitive development of school-age survivors of HLHS (6–16 years of age) was below normal: 25.5% were in the 'far below normal' range and 27.9% in the 'below normal' range. Nevertheless, almost 50% of these patients achieved results in or above the normal range. Two out of the 43 tested children even reached values in the 'far above normal' range, indicating that HLHS patients have the potential of cognitive development comparable to that of the normal population.

Looking into more detail, it was interesting to find out that while the results in verbal communication, perceptual reasoning and processing speed conformed to the total index results and, thus, were lower than the average of the age-adjusted normative values, the results in working memory were better and in the average range of normal results. Based on this finding, it can be assumed that in this group of patients, the skills necessary for working memory (attention and concentration, short-term memory) can be acquired and improved through effectual training and intensive help from parents, so that these children no longer show performance differences as compared to the rest of the population. We think that this information can be of great importance for postoperative management, rehabilitation, and parental counseling.

A review of other studies [27–32] has shown that there is no comprehensive and detailed data concerning the cognitive development of schoolchildren of ages up to 17 with HLHS. Knirsch et al. [27] have shown by means of the Wechsler Primary Preschool Intelligence Scale-II and the Movement-ABC 2 that preschoolers with a Fontan procedure show slightly substandard cognitive intelligence scores [median IQ 89 (76–116), $p = 0.02$]. Using the same measurement tools, Hansen et al. [28] have shown results for preschool children (3.5–6.8 years) in the lower-normal range. In summarizing the current state of knowledge related to neurodevelopmental outcomes for children with HLHS, Goldberg et al. have shown that children with HLHS who have survived stages of Fontan palliation can have normal developmental outcomes, but nonetheless are at significant risk for learning disorders, lowered academic achievement, and behavioral abnormalities. Puosi et al. [30] and Williams et al. [31] obtained their findings from very small trial groups ($n = 4$, $n = 22$) of HLHS children ages 18 months and 2 years, respectively, and confirmed a significantly lower mean mental development index, more delays in expressive language functions, and more behavioral problems than in the control group. Via questionnaire, Mahle et al. [32] collected data from school-aged survivors with HLHS (mean age 8.6 ± 2.1 years) concerning their quality of life, school performance, and incidence of medical complications. A subgroup of local patients ($n = 28$) underwent standardized testing of cognitive function and neurologic examination. Cognitive testing of these children demonstrated a median full scale IQ of 86 (range 50–116). Mental retardation (IQ < 70) was noted in 18% of patients. In multivariate analysis, only the occurrence of preoperative seizures predicted lower full scale IQ.

Referring to results of patients with single ventricle after-Fontan procedures (median age 11.1, range 3.7–41.0 years), Wernovsky et al. [12] have shown that most individual patients palliated with Fontan procedures in the 1970s and 1980s have cognitive outcomes and academic function within the normal range, but the performance of the cohort is lower than that of the general population.

Our own study's results underscore Mahle's [32] conclusion: "Although the majority of school-aged children with HLHS scores within the normal IQ range, mean performance for historical cohort of survivors was lower than that in the general population," however, in a more differentiated manner:

Cognitive Performance in Relation to Risk Factors

Delayed neurodevelopment has already been reported in children operated for severe congenital left heart disease. However, it is still unclear what impact abnormal intrauterine brain development has versus postnatal insults due to long-lasting cardiopulmonary bypass, brain perfusion, and hemodynamic instabilities in the pre- and postoperative courses.

Prenatal diagnosis offers the possibility of a planned delivery and prenatal management, thus avoiding acidosis and hemodynamic instabilities. It has been speculated that a prenatal diagnosis will lead to better survival and surgical outcomes and might have an impact on neurodevelopmental outcomes, as well. Almost half of the patients tested in this study had been given a prenatal diagnosis. Although prenatally diagnosed patients had better scores in total and all other subscales, there was no significant difference in any of the tested indices.

Anatomy

Abnormal brain development in HLHS patients has been linked to retrograde arch perfusion with lower oxygenated blood from the right ventricle. Therefore, fetuses with aortic stenosis and some residual antegrade arch perfusion are thought to have a better cerebral oxygen concentration and brain perfusion. Our results did not reveal any significant differences between the 2 groups.

Shunt Types

When our patients with modified Blalock–Taussig shunts were compared to the patients with Sano-shunts, we found significantly better results in the Sano group regarding verbal comprehension and perceptual reasoning. The time of the Norwood operation is a critical period in the life of hypoplastic left heart syndrome patients. It still carries significant mortality and morbidity. Postoperative hemodynamic instability is frequent and may be associated with impaired brain perfusion. Use of a 5-mm Sano-shunt (right ventricle to pulmonary artery conduit) instead of a modified Blalock–Taussig shunt is thought to lead a more stable circulation in the early postoperative period.

Perfusion Techniques

Over the study period, different perfusion techniques were used during the Norwood operation to optimize brain and end-organ perfusion. When we compared deep hypothermic circulatory arrest (which we used in the first five patients) to the ten patients who had selective antegrade cerebral perfusion as well as to the 28 last patients on whom a double perfusion technique had been performed, we did not find significant differences in any of the tested cognitive parameters, but the numbers were small for each group. Positive trends toward an improved performance were found in the cerebral perfusion and double perfusion group versus the circulatory arrest group. This would support the concept that low flow is better for the brain than no flow.

Learning Curve/Surgery Timeline

In view of the fact that a number of improvements, especially in surgical techniques, surgeon skills, intensive-care unit teams, perfusion techniques, and patient management have taken place since 1997, we expected a positive effect on cognitive outcomes in patients who were treated in the second half of the study period. Although we found that the results in total, verbal comprehension, and perceptual reasoning rose from below average to average after 2004 (above the index value of 85), no significant differences in all tested parameters were found.

Gender

The intelligence quotient index in verbal comprehension of boys was—as opposed to the scores of boys within the total population—*significantly better*. The indices for perceptual reasoning, working memory, and the total score showed male HLHS patients ahead of the others, however, outside of the significance level. In processing speed, HLHS males showed nearly equal results. Interestingly, this runs contrary to current research findings for the total population concerning the development of boys and girls. We have no explanation for this [25].

School and Parents' Education

Whenever parents evaluated their child's teacher–student relationship as excellent, these children achieved *significantly better*

results in cognitive areas, especially in verbal comprehension. Additionally, we were able to show that children whose parents had higher education levels performed significantly better.

This also provides some evidence that HLHS children can be schooled and educationally supported similar to healthy children. Obviously, this can be achieved through both higher parental education levels as well as the public school system. It was interesting to see that three of the HLHS survivors even achieved above-average results: two of them had a prenatal diagnosis, all had antegrade cerebral perfusion, all a Sano-shunt, and their parents were well educated and highly supportive. This suggests that not one single factor but a combination of all relevant factors are most likely responsible for favorable neurodevelopment.

Limitations

The major limitation of this study is the small sample size. Several parameters might become significant with larger patient numbers, which would only be possible to assess by looking at multicenter studies. One strength of this study, however, is that all patients were treated at the same center and that all stage I Norwood procedures were performed by only one single surgeon (RM). Another limitation is the retrospective analysis of the anatomy and the clinical course, which involved at least three surgeries. Further alternatives of analysis (multivariate methods) are limited due to the small sample.

Due to the small trial group ($n = 43$), several correlations were not shown in a statistically significant manner. However, we demonstrated the following trends and tendencies that are encouraging in terms of differentiated treatment of HLHS patients:

(1) Significantly better results in the Sano group regarding verbal comprehension and perceptual reasoning.
(2) Positive trends toward an improved performance in the cerebral perfusion and double perfusion group versus the circulatory arrest group. This would support the concept that low flow is better for the brain than no flow.
(3) We found that the results in total, for verbal comprehension, and in perceptual reasoning rose from below average to average after 2004 (above the index value of 85).

Conclusions

School-age survivors of HLHS had an average cognitive development below normal. However, almost 50% of these patients achieved results in the normal or even above-normal range. Only the results in working memory (attention, concentration, short-term memory) were in the average range. Significant factors associated with better cognitive development were: Sano-shunt at the time of Norwood operation, an excellent student–teacher relationship and parents with higher education. It can be assumed that the skills necessary for working memory can be acquired and improved through effective training. Advances in surgical and perfusion techniques might further contribute to better cognitive development of such patients. Pedagogical and educational support can help these children and their families live successful lives and to achieve the full developmental potential of patients with HLHS.

Perspectives/Translational Outlook

Children with HLHS can achieve successful school careers. Appropriate tutoring and the individual development of resilient personality traits can positively impact cognitive development.

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Compliance with Ethical Standards

Conflicts of interest All authors declare that they have no conflict of interest.

Ethical Approval The authors hereby state that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines—IRB (ID-number J16-01), ethical review committee—and have been approved by the institutional committee.

References

1. Li Y, Yin S, Fang J et al (2015) Neurodevelopmental delay with congenital heart disease is mainly from prenatal injury not infant cardiac surgery, current evidence based on a meta-analysis of functional magnetic resonance imaging. Ultrasound Obstet Gynecol 45:639–648
2. Mahle WT et al (2001) Impact of prenatal diagnosis on survival and early neurologic morbidity in neonates with hypoplastic left heart syndrome. Pediatrics 107:1277
3. Mahle WT et al (2004) Neurodevelopmental outcomes in hypoplastic left heart syndrome. Pediatr Card Surg Annu 7:39–47
4. Paquetta LB et al (2013) Abnormal cerebral microstructure in premature neonates with cognitive heart disease. Am J Neuroradiol 34:2026
5. Rychik J (2005) Hypoplastic left heart syndrome: from in utero diagnosis to school age. Seminars Fetal Neonatal Med 10:553–566
6. Mahle WT (2013) A predictive model for neurodevelopmental outcome after the Norwood procedure. Pediatr Cardiol 34:327–333
7. Gaynor JW et al (2013) Neurodevelopmental outcomes in preschool survivors of the Fontan procedure. J Thorac Cardiovasc Surg 147:1276–1282

8. Hoffmann GM (2013) Perioperative cerebral oxygen saturation in neonates with hypoplastic left heart syndrome and childhood neurodevelopmental outcome. J Thorac Cardiovasc Surg 146:1153–1164
9. Lambert LM et al (2009) Parent versus child reported functional health status after Fontan procedure. Pediatrics 124:e942–e949
10. Rychik J (2014) Hypoplastic left heart syndrome: can we change the rules of the game? Circulation 130:629–631
11. Tabbutt S et al (2008) Neurodevelopmental outcomes after staged palliation for hypoplastic left heart syndrome. Pediatrics 121:476–483
12. Wernovsky G et al (2000) Cognitive development after the Fontan operation. Circulation 102:189–193
13. Brosig CL et al (2013) Neurodevelopmental outcomes for children with hypoplastic left heart syndrome at the age of 5 years. Pediatr Cardiol 3:1597–1604
14. Brosig CL et al (2007) Psychosocial outcomes for preschool children and families after surgery for complex congenital heart disease. Pediatr Cardiol 28:255–262
15. Brosig CL et al (2007) Neurodevelopmental outcomes in preschool survivors of complex congenital heart disease: implications for clinical practice. J Pediat Health Care 21:3–12
16. Kramer HH (2006) Development of personality and intelligence in children with congenital heart disease. J Child Psychol Psychiat 30:299–308
17. Rychik J et al (2014) Late consequences of the Fontan operation. Circulation 130:1525–1528
18. Sarajuuri A et al (2012) Neurodevelopmental burden at age 5 years in patients with univentricular heart. Pediatrics 130:1636–1646
19. Peterlechner T (2007) Das Hypoplastische Linksherz-Syndrom. Aktuelle diagnostische und therapeutische Strategien und Outcome am Kinderherzzentrum Linz unter Berücksichtigung des Einflusses von Diagnosezeitpunkt und präoperativen Risikofaktoren. Unveröffentlichte Dissertation. Universität Innsbruck
20. Wechsler D (2004) The Wechsler intelligence scale for children. Pearson, London
21. Mayring P (2003) Qualitative inhaltsanalyse. Beltz, Weinheim
22. Kline RB (2013) Beyond significance testing: reforming data analysis methods in behavioral research. Am Psychol Assoc, Washington
23. Ohyle RG, Seeper LA, Mahony L et al (2010) Comparison of shunt types in the Norwood procedure for single-ventricle lesions. N Engl J Med 362(21):1980–1992
24. Raja SG, Atamanyuk I, Kostolny M et al (2009) In hypoplastic left heart patients is Sano shunt compared with modified Blalock–Taussig shunt associated with deleterious effects on ventricular performance? Interact Cardiovasc Thorac Surg 10(4):620–624
25. Halpern D (2013) Sex differences in cognitive abilities. Psychology Press, New York
26. Law M et al (2014) Health related quality of life of children with physical disabilities: a longitudinal study. BMC Pediatrics 26:1–10
27. Knirsch W et al (2016) Neurodevelopmental outcome of children with hypoplastic left heart syndrome at one and four years of age comparing hybrid and Norwood procedure. Ann Thorac Cardiovasc Surg 22:375–377
28. Hansen JH et al (2016) Neurodevelopmental outcome in hypoplastic left heart syndrome: impact of perioperative cerebral tissue oxygenation of Norwood procedure. J Thorac Cardiovasc Surg 151(5):1358–1366
29. Goldberg C et al (2011) Neurodevelopment and quality of life for children with hypoplastic left heart syndrome: current knowns and unknowns. Cardiol Young 21(2):88–92
30. Puosi R et al (2011) Neurocognitive developent and behavioral outcome of 2-year-old children with univentricular heart. J Int Neuropsychol Soc 17(6):1094–1103
31. Williams IA et al (2012) Fetal cerebrovascular resistance and neonatal EEG predict 18-month neurodevelopmental outcome in infants with congenital heart disease. Ultrasound Obstet Gynecol 40(3):304–309
32. Mahle WT et al (2000) Neurodevelopmental outcome and lifestyle assessment in school-aged and adolescent children with hypoplastic left heart syndrome. Pediatrics 105(5):1082–1089