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Neurodevelopmental Outcomes at 2 Years and 4 Years in Children with Congenital Heart Disease

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Abstract

Background and Objectives—Children with congenital heart disease (CHD) are at risk for neurodevelopmental (ND) delays. The purpose of this study is to compare the ND testing results of children with CHD at 2 and 4 years of age and determine if rates of ND delays change over time.

Methods—Children with CHD completed the Bayley Scales of Infant Development – III (BSID-III) at 2 years of age, and standardized neuropsychological measures at 4 years. Scores were compared to test norms and were classified as: average (within one SD of test mean); at risk (1-2 SDs from the test mean); and delayed (>2SD from test mean). Pearson correlations and McNemar's exact tests were performed to determine the relationship between test scores at the two times of assessment.

Results—Sixty-four patients completed evaluations at 24±3 months of age and 4 years of age. BSID-III cognitive and fine motor scores were correlated with preschool IQ and fine motor scores,

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Author Contributions:

Cheryl L. Brosig: Dr. Brosig conceptualized and designed the study, completed the 4 year old developmental evaluations of the subjects enrolled, assisted with subject recruitment and informed consent, supervised data collection, prepared data for analysis, led interpretation of results, prepared the manuscript, and approved the final manuscript as submitted.

Laurel Bear: Dr. Bear contributed to study design, provided oversight of the 2 year old developmental evaluations of the subjects enrolled, assisted with subject recruitment and informed consent, reviewed and revised the manuscript, and approved the final manuscript as submitted.

Sydney Allen: Ms. Allen contributed to study design, assisted with design of the database and data collection tools, collected and entered data, reviewed and revised the manuscript, and approved the final manuscript as submitted.

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Liyun Zhang: Ms. Zhang carried out the statistical analysis, contributed to interpretation of results, reviewed and revised the manuscript, and approved the final manuscript as submitted.

Michele Frommelt: Dr. Frommelt contributed to study design, reviewed and revised the manuscript, and approved the final manuscript as submitted.

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$r = 0.75$ to 0.87 , $p < 0.0001$. Agreement in score categories was 79% for cognitive and 61% for fine motor. More patients had at risk or delayed scores at age 4 vs. age 2 ($p \leq 0.01$).

Conclusion(s)—Despite significant correlations between 2 and 4 year old test scores, many patients who scored in the average range at age 2 showed deficits at age 4. BSID-III scores at age 2 may underestimate delays. Therefore, longitudinal ND assessment is recommended.

Keywords

congenital heart disease/defects; developmental follow-up; developmental outcomes; assessment & surveillance; child development

Introduction

Children with congenital heart disease (CHD) are at risk for a characteristic pattern of neurodevelopmental (ND) problems that includes deficits in language, motor, executive functioning, and social skills. [1–11] Notably, ND problems in survivors of CHD are more common than late mortality, significant arrhythmias, or bacterial endocarditis, and thus represent the most common long-term morbidity in these patients. [4] Because of the high prevalence of these deficits, and their impact on quality of life, the American Heart Association (AHA) and the American Academy of Pediatrics (AAP) now recommend systematic evaluation of development in children with CHD throughout childhood to promote early detection of delays and optimize outcomes.[1] Cardiac centers have begun to incorporate developmental follow-up programs as part of routine cardiac care.[12–14] However, few centers have reported outcomes for patients seen in these programs, and little is known about whether early developmental evaluations performed in these clinics can predict later outcomes.

We have previously reported developmental outcomes of children who were evaluated in our longitudinal developmental follow-up program over the first 3 years of life, and found that delays were common, but the pattern of delays changed over time. [15, 16] We have also reported ND outcomes for preschool-aged children seen in our program, and found that deficits for preschoolers with CHD without genetic conditions were mild, and may not be detected without formal testing. [17] The aim of this study was to investigate the relationship between ND test scores at 2 years and 4 years of age, and determine whether rates of ND problems change over time, and whether developmental evaluations at age 2 could predict ND outcomes at age 4.

Methods

Patient Population

Children with CHD believed to be at high risk for developmental delay as defined by the AHA/AAP guideline[1], were recruited from the Herma Heart Center Developmental Follow-up Clinic (HHCDC) at Children's Hospital of Wisconsin (CHW, Figure 1). Eligibility criteria and operation of the HHCDC have been previously described.[12,15–17] Children with CHD were seen for serial developmental evaluations, approximately every 6 months, between 6 months and 3 years of age. Families were then contacted by letter to

schedule a subsequent developmental evaluation when the child reached 4-6 years of age. Children were seen for ND testing within the cardiology clinic; appointments lasted approximately 2-3 hours, depending on the child's age. To be eligible for this study, children had undergone a preschool ND evaluation, as well as a developmental evaluation at 24 ± 3 months of age. Parents provided informed consent to have their child's data included in a databank approved by the Institutional Review Board at CHW. No subjects were excluded based on race or other coexisting medical or genetic condition. Children who did not speak English were not included, as tests needed to be administered in English.

Measures

At the 24 ± 3 month of age assessment, children completed the Bayley Scales of Infant and Toddler Development, Third Edition (BSID-III).[18] The BSID-III provides composite scores for cognitive, language, and motor skills (mean = 100, SD = 15), as well as subscale scores for expressive and receptive language, and fine and gross motor skills (mean = 10, SD = 3). At the preschool visit, children completed a comprehensive ND battery [17]. The Wechsler Preschool and Primary Scale of Intelligence, Third or Fourth Edition (WPPSI-III, WPPSI-IV) [19, 20] Full Scale Intellectual Quotient (IQ) score (mean = 100, SD = 15) was used as a preschool measure of cognitive skills. The Pegboard subtest scaled score (mean = 10, SD = 3) of the Wide Range Assessment of Visual Motor Abilities (WRAVMA) [21] was used as a preschool measure of fine motor skills. For purposes of this study, the cognitive composite score of the BSID-III was compared with the WPPSI Full Scale IQ score; the fine motor subscale score of the BSID-III was compared with the WRAVMA Pegboard score.

Parents completed a basic demographic form which provided information about parental education and occupation, as well as family structure and the child's history of participation (past or present) in early intervention services (speech, physical and/or occupational therapy). Information regarding patient and treatment characteristics was abstracted from the medical record.

Statistical Analysis

Sample characteristics and clinical variables are presented as medians with interquartile range (IQR) for continuous data and frequencies (%) for categorical data. ND test scores were converted to standard Z scores based on test norms/standard deviations (SDs). Age 2 and age 4 two-paired scores were compared by using Wilcoxon Signed Rank tests. Scores were classified as: normal (within 1 SD of test mean); at risk (1-2 SDs from test mean); or delayed (>2 SDs from test mean). Pearson correlations were used to examine the linear relationship between raw test scores at age 2 and age 4. A McNemar's exact test was used to examine the change in score classification from age 2 to age 4. Sensitivities, specificities, and positive and negative predictive values were calculated with 95% exact Clopper Pearson intervals. A two-sided p-value of <0.05 was considered as significant. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, North Carolina) software.

Results

From March 2011 through August 2016, 141 subjects with pediatric heart disease completed preschool ND testing (Figure 1). Of these, 105 (74.5%) had been seen in the 0 to 3 clinic; 64 (45.4%) had a developmental evaluation at 24 ± 3 months of age.

Characteristics of the sample are presented in Table 1. Median age at preschool assessment was 4.4 years (IQR 4.3 – 4.7 years). Anatomy was classified according to the child's fundamental diagnosis at birth. Thirty percent of the subjects had anatomy that required surgical palliation resulting in a functional single ventricle (1V). Twenty-three percent (n=15) of the subjects had a known medical comorbidity, in addition to their CHD, involving the following systems: airway (n=7), gastrointestinal/genitourinary (n=2), hearing (n=1), neurologic (n=1), chronic lung disease (n=1), multisystem (n=2), orthopedic (n=1). Twenty-two percent (n=14) of the subjects had a diagnosed genetic condition: trisomy 21 (n=6); 22q11 deletion (n=2); Turner syndrome (n=2); chromosomal deletion (n=1); Williams syndrome (n=1); Barth syndrome (n=1); Pierre Robin syndrome (n=1). Of these, 12/14 children had two ventricle (2V) anatomy. One subject with double inlet left ventricle had Pierre Robin syndrome; one subject with tricuspid atresia had Williams syndrome.

Subject and treatment characteristics at the time of assessment are presented in Table 2. All subjects had undergone a surgical or catheter based cardiac intervention within the first year of life, making them eligible for the developmental follow-up program. The majority of subjects, 59/64 (92%) had undergone at least one heart surgery requiring cardiopulmonary bypass (CPB), and 24/64 (38%) had undergone deep hypothermic circulatory arrest (DHCA). A majority of subjects, 59/64 (92%), had received early intervention services (e.g., physical, occupational or speech therapy) previously, but only 29/64 (45%) were currently enrolled in early intervention services at the time of their preschool evaluation.

The mean BSID-III cognitive composite score at age 2 was 94.5 (SD = 21.2). The mean WPPSI-III/IV Full Scale IQ score at age 4 was 93.1 (SD = 21.1). Scores were significantly correlated; Pearson $r=0.80$, $p<0.0001$. The mean BSID-III fine motor scaled score (age 2) was 9.6 (SD=3.7). The mean WRAVMA Pegboard standard score (age 4) was 86.4 (SD = 18.6). Scores were significantly correlated, Pearson $r=0.75$, $p<0.0001$.

The percentages of the subjects that fell within the average (within 1SD of test norm), at-risk (1-2 SD from test norm) and delayed (>2 SD from test norm) ranges at age 2 versus age 4 are illustrated in Figure 2 (cognitive scores) and Figure 3 (fine motor scores). There was 78.6% agreement in cognitive score categories (average, at risk, delayed); more patients were at risk at age 4 vs. age 2 ($p=0.007$). There was 61% agreement in fine motor score categories; more patients were at risk or delayed at age 4 vs. age 2 ($p<0.001$). At both age 2, and age 4, there were more children in the delayed category for cognitive scores if they had a genetic condition ($p<0.0001$). For fine motor scores, at age 2, there were more children in the average category if they had no/other medical conditions compared to those who had a genetic condition ($p<0.0001$). At age 4, for fine motor scores, there were more children in the delayed category if they had a genetic condition.

Sensitivities, specificities, and positive and negative predictive values were calculated and are reported in Table 3. The positive predictive value of a BSID-III score that was at risk or delayed ($>1SD$ below the mean) to predict a similar score at age 4 was 100% for both cognitive and fine motor skills. For children who scored in the at risk or delayed range at age 4, the sensitivity of the BSID-III to detect a similar delay at age 2 was 33% with 95% C.I. (15.6%, 55.3%) for fine motor and 50% with 95% C.I. (28.2%, 71.8%) for cognitive skills.

Discussion

Consistent with previous research on ND outcomes in children with CHD[15, 16, 22, 23], results of the current study indicate that rates of delay for children with CHD change over time. Although there were statistically significant correlations between scores at age 2 and age 4, more children in the current study fell in the at risk or delayed category at age 4 compared to age 2 for both cognitive and fine motor skills. This is in contrast to findings from other studies that found improved cognitive scores over time [24, 25]. Creighton et al. [24] studied neurocognitive outcomes in children with complex congenital heart disease at age 2 and age 5 and found that fewer children were delayed at 5 years than at 2 years. These findings may differ from the current study due to the use of different ND measures. In addition, Creighton et al. [24] excluded patients with chromosomal abnormalities, whereas the current study included scores from these children. Because children with CHD and comorbid genetic conditions do meet the AHA/AAP[1] criteria regarding which children should be referred for repeated ND assessment, we felt that it was important to include them in our results.

Bode et al. [25] studied cognitive outcomes at 2 and 4 years of age in children who were born preterm and concluded that the BSID-III administered at 2 years of age is a good predictor of cognitive function at 4 years. Of the children who changed score categories over time, most moved into an improved category, in contrast to the current study in which most children that changed categories moved into a worse category. It is possible that the developmental trajectories for children born preterm compared to children with CHD may differ because the groups have different medical experiences between 2 and 4 years of age. Patients from the current study may have been exposed to further developmental risk between age 2 and 4 due to abnormal cardiac function, additional open heart surgeries, time on cardiopulmonary bypass, days in the hospital, etc., which may have negatively impacted their ND scores.

Results of the current study suggest that delays detected by the BSID-III at age 2 likely reflect “true” delays that continue to age 4. However, the sensitivity of the BSID-III was only 33% for fine motor skills and 50% for cognitive skills, suggesting that the BSID-III has a high rate of false negatives. This is consistent with other studies that have shown that the BSID-III underestimates rates of delay when compared to earlier versions of the measure [26, 27]. Parents and practitioners should be cautioned that an average score on the BSID-III does not rule out the possibility for later delays. Because some problems in children with CHD may not present until later childhood or adolescence (e.g., deficits in executive functioning, social cognition), comprehensive, longitudinal ND assessment is recommended.

There are some important limitations to the current study. Results are based on a small sample size from a single center; thus, results may not generalize to the CHD population as a whole. In addition, we were not able to quantify additional factors that occurred between the two ND assessments that may have exposed patients to further developmental risk. Finally, a high percentage of patients had participated in early intervention services in the past, and almost half of them were receiving early intervention services at the time of the 4 year old assessment; what impact those services had on ND outcomes is not known.

Conclusions

Children with CHD are at risk for ND delays. In this study, rates of ND delay changed over time, with more children showing problems at age 4 years compared to age 2 years. Providers should counsel parents about the importance of comprehensive, longitudinal ND follow-up in this high risk population.

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Abbreviations

1V	single ventricle
2V	two ventricles
AAP	American Academy of Pediatrics
AHA	American Heart Association
BSID-III	Bayley Scales of Infant Development – III
CHD	congenital heart disease
CHW	Children’s Hospital of Wisconsin
CPB	cardiopulmonary bypass
DHCA	deep hypothermic circulatory arrest
GA	gestational age
HHCDC	Herma Heart Center Developmental Follow-Up Clinic
IQ	intellectual quotient
IQR	interquartile range

ND	neurodevelopmental
SD	standard deviation
WPPSI	Wechsler Preschool and Primary Scales of Intelligence
WRAVMA	Wide Range Assessment of Visual Motor Abilities

References

1. Marino BS, Lipkin PH, Newburger JW, et al. American Heart Association Congenital Heart Defects Committee, Council on Cardiovascular Disease in the Young, Council on Cardiovascular Nursing, and Stroke Council. Neurodevelopmental outcomes in children with congenital heart disease: evaluation and management: a scientific statement from the American Heart Association. *Circulation*. 2012; 126:1143–1172. [PubMed: 22851541]
2. Snookes SH, Gunn JK, Eldridge BJ, et al. A systematic review of motor and cognitive outcomes after early surgery for congenital heart disease. *Pediatrics*. 2010; 125:e818–e827. [PubMed: 20231182]
3. Cassidy AR, White MT, DeMaso DR, Newburger JW, Bellinger DC. Executive function in children and adolescents with critical cyanotic congenital heart disease. *J Int Neuropsychol Soc*. 2015; 21:34–49. [PubMed: 25487044]
4. Wernovsky G. Current insights regarding neurological and developmental abnormalities in children and young adults with complex congenital cardiac disease. *Cardiol Young*. 2006; 16(suppl 1):92–104.
5. Bellinger DC, Wypij D, Rivkin MJ, et al. Adolescents with d-transposition of the great arteries corrected with the arterial switch procedure: neuropsychological assessment and structural brain imaging. *Circulation*. 2011; 124:1361–1369. [PubMed: 21875911]
6. Sananes R, Manlhiot C, Kelly E, et al. Neurodevelopmental outcomes after open heart operations before 3 months of age. *Ann Thorac Surg*. 2012; 93:1577–1583. [PubMed: 22541188]
7. Brosig C, Mussatto K, Hoffman G, et al. Neurodevelopmental outcomes for children with hypoplastic left heart syndrome at the age of 5 years. *Pediatr Cardiol*. 2013; 34:1597–1604. [PubMed: 23503929]
8. Calderon J, Angeard N, Pinabiaux C, Bonnet D, Jambaque I. Facial expression recognition and emotion understanding in children after neonatal open-heart surgery for transposition of the great arteries. *Dev Med Child Neurol*. 2014; 56:564–571. [PubMed: 24444170]
9. Ricci MF, Andersen JC, Joffe AR, et al. Chronic neuromotor disability after complex cardiac surgery in early life. *Pediatrics*. 2015; 136:e922–e933. [PubMed: 26391946]
10. Gerstle M, Beebe D, Drotar D, Cassedy A, Marino B. Executive functioning and school performance among pediatric survivors of complex congenital heart disease. *J Pediatr*. 2016; 173:154–159. [PubMed: 26875011]
11. Sanz J, Berl M, Armour A, Wang J, Cheng Y, Donofrio M. Prevalence and pattern of executive dysfunction in school age children with congenital heart disease. *Con Heart Dis*. 2016; doi: 10.1111/chd.12427
12. Brosig Soto C, Olude O, Hoffmann RG, et al. Implementation of a routine developmental follow-up program for children with congenital heart disease: early results. *Con Heart Dis*. 2011; 6:451–460.
13. Brosig CL, Butcher J, Butler S, et al. Monitoring developmental risk and promoting success for children with congenital heart disease: Recommendations for cardiac neurodevelopmental follow-up programs. *Clin Pract Pediatr Psychol*. 2014; 2:153–165.
14. Chorna O, Baldwin HS, Neumaier J, et al. Feasibility of a team approach to complex congenital heart defect neurodevelopmental follow-up: Early experience of a combined cardiology/neonatal intensive care unit follow-up program. *Circ Cardiovasc Qual Outcomes*. 2016; 9:432–440. [PubMed: 27220370]

15. Mussatto KA, Hoffmann RG, Hoffman GM, et al. Risk and prevalence of developmental delay in young children with congenital heart disease. *Pediatrics*. 2014; 133:e570–e577. [PubMed: 24488746]
16. Mussatto KA, Hoffmann R, Hoffman G, et al. Risk factors for abnormal developmental trajectories in young children with congenital heart disease. *Circulation*. 2015; 132:755–761. [PubMed: 26304667]
17. Brosig CL, Bear L, Allen S, et al. Preschool neurodevelopmental outcomes in children with congenital heart disease. *J Pediatr*. 2017; 183:80–86. [PubMed: 28081891]
18. Bayley N. The Bayley Scales of Infant Development-III. San Antonio, TX: The Psychological Corporation; 2006.
19. Wechsler D. Wechsler Preschool and Primary Scale of Intelligence Administration and Scoring Manual. 3rd. San Antonio, TX: The Psychological Corporation; 2002.
20. Wechsler D. Wechsler Preschool and Primary Scale of Intelligence Administration and Scoring Manual. 4th. Bloomington, MN: NCS Pearson, Inc; 2012.
21. Adams W, Sheslow D. Wide Range Assessment of Visual Motor Abilities Manual. Lutz, FL: Psychological Assessment Resources, Inc; 1995.
22. Bellinger D, Wypij D, duPleiss A, et al. Neurodevelopmental status at eight years in children with dextro-transposition of the great arteries: The Boston Circulatory Arrest Trial. *J Thorac Cardiovasc Surg*. 2003; 126:1385–1396. [PubMed: 14666010]
23. McGrath E, Wypij D, Rappaport L, Newburger J, Bellinger D. Prediction of IQ and achievement at age 8 years from neurodevelopmental status at age 1 in children with D-transposition of the great arteries. *Pediatrics*. 2004; 114:e572–e576. [PubMed: 15492354]
24. Creighton D, Robertson C, Sauve R, et al. Western Canadian Complex Pediatric Therapies Follow-Up Group. Neurocognitive, functional, and health outcomes at 5 years of age for children after complex cardiac surgery at 6 weeks of age or younger. *Pediatrics*. 2007; 120:e478–e486. [PubMed: 17766491]
25. Bode M, D'Eugenio D, Mettelman B, Gross S. Predictive validity of the Bayley, Third Edition at 2 years for intelligence quotient at 4 years in preterm infants. *J Dev Behav Pediatr*. 2014; 35:570–575. [PubMed: 25370298]
26. Acton B, Biggs W, Creighton D, et al. Overestimating neurodevelopment using the Bayley-III after early complex cardiac surgery. *Pediatrics*. 2011; 128:e794–e800. [PubMed: 21949148]
27. Anderson P, DeLuca C, Hutchinson E, et al. Underestimation of developmental delay by the new Bayley-III scale. *Arch Pediatr Adolesc Med*. 2010; 164:352–356. [PubMed: 20368488]

Figure 1. Herma Heart Center Developmental Follow-up Clinic (HHCDC) patients. Shaded box identifies current study cohort. CHD, congenital heart disease; ND, neurodevelopmental.

Figure 2.
Percent of patients in the average, at risk, or delayed range for cognitive scores at age 2 years versus age 4 years.

Figure 3.
Percent of patients in the average, at risk, or delayed range for fine motor scores at age 2 years versus age 4 years.

Table 1

Sample Demographics N = 64

Demographics	n (%)
Sex: Male	40 (63)
Race/ethnicity	
White, Non-Hispanic	41 (64)
Other	22 (34)
Missing	1 (2)
Maternal education	
Post-High School	48 (75)
High school or less	10 (16)
Missing	6 (9)
Family constellation	
Married	42 (66)
Single	12 (19)
Other	7 (11)
Missing	3 (5)
Prenatal diagnosis: Yes	33 (52)
Premature: GA ^I <37 wks	10 (16)
Anatomy	
Two Ventricle	41 (64)
Single ventricle	19 (30)
Cardiomyopathy	4 (6)
Comorbidities	
None	35 (55)
Other medical	15 (23)
Genetic	14 (22)

^IGA, gestational age

Table 2**Subject and Treatment Characteristics**

	Median	Interquartile Range (25th-75th percentile)
Age at first cardiac surgery, days	20	8-90
Length of hospitalization, days ^a	48	25-86
CPB time, minutes ^{a,b}	217	136-348
DHCA time, minutes ^{a,c}	12	8-24
Early intervention (past, 0-3 years old)	Yes = 92%	
Early intervention (current, 4 years old)	Yes = 45%	

CPB, cardiopulmonary bypass; DHCA, deep hypothermic circulatory arrest.

^aCumulative to the time of 4 year ND assessment.

^b5 subjects never had open heart surgery.

^c24 subjects had DHCA.

Table 3

Prediction of the Bayley Scales of Infant Development-III at Age 2 years on 4 Year Neurodevelopmental Scores

At risk or delayed	Positive Predictive Value, % and 95% C.I.	Negative Predictive Value, % and 95% C.I.	Sensitivity, % and 95% C.I.	Specificity, % and 95% C.I.
Cognitive	100.0 (71.5, 100.0)	75.6 (60.5, 87.1)	50.0 (28.2, 71.8)	100.0 (89.7, 100.0)
Fine motor	100.0 (63.1, 100.0)	68.6 (54.1, 80.9)	33.0 (15.6, 55.3)	100.0 (90.0, 100.0)

C.I., confidence interval