Cohort and Individual Neurodevelopmental Stability between 1 and 6 Years of Age in Children with Congenital Heart Disease

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Objective To assess cohort and individual neurodevelopmental stability in children with congenital heart disease across childhood.

Study design The Reachout Study is a cohort study at the University Children's Hospital Zurich. Data from 148 children with congenital heart disease who underwent cardiopulmonary bypass surgery and 1-, 4-, and 6-year neurodevelopmental assessment were analyzed using mixed models.

Results Cognitive and motor functions of the total cohort improved over time (cognitive: $P = .01$; motor: $P < .001$). The prevalence of children with cognitive impairment at age 6 years was 22.3%. Socioeconomic status showed a significant interaction with age on cognitive and motor development (cognitive: $P < .001$; motor: $P = .001$): higher socioeconomic status was associated with better neurodevelopmental outcome over time. Weight and head circumference at birth showed a significant interaction with age on motor development (weight: $P = .048$; head: $P = .006$). The correlation between test scores at different ages was weak to moderate (cognition: age 1-6 years: rho = 0.20, age 4-6 years: rho = 0.56, motor: age 1-6 years: rho = 0.23, age 4-6 years: rho = 0.50).

Conclusions Children with congenital heart disease show a mild improvement in cognitive and motor functions within the first 6 years of life, particularly those with higher socioeconomic status and larger head circumference and weight at birth. However, individual stability is moderate at best. Therefore, follow-up assessments are crucial to target therapeutic intervention effectively. *(J Pediatr 2019;215:83-9)*.

Children who have undergone infant cardiopulmonary bypass surgery because of congenital heart disease (CHD) are at risk for delays in several developmental domains,[1] and neurodevelopmental delays have been described persisting into school age and adolescence.[2,3] However, it is still unclear how these deficits evolve over time. Although some problems arise early on, others only emerge during school age because of later maturation of executive function, reading, writing, and mathematical skills.[1] When investigating the evolution of such deficits, longitudinal studies are essential.

To date, 2 studies have presented longitudinal data assessing comparable outcome measures over time to define neurodevelopment in children with CHD. Both reported improvement with age in cognitive and motor functions in early childhood (3 years of age) and found these improvements to be modified by factors such as a single ventricle defect and genetic disorder.[4-6] Thus, cognitive and motor development may vary substantially among children, making the prediction of later outcome difficult for an individual child.

Previous studies have presented prediction models derived from cohorts of patients with CHD and identified risk factors for poor outcome for the entire cohort.[7,8] In contrast, neurodevelopmental stability is rarely described.[9] However, both prediction models and neurodevelopmental stability should be considered when counselling parents about future outcome. Further, studies in healthy children have shown that individual stability might be low in early childhood but becomes higher with increasing age.[10]

We evaluated neurodevelopment in an at-risk population of children with CHD by assessing cognitive and motor functions at 3 time points across childhood. We consider both cohort and individual stability.

Methods

The Reachout Study is a longitudinal cohort study at the University Children's Hospital in Zurich. Children with CHD who underwent cardiopulmonary bypass surgery between 2004 and 2009 were prospectively enrolled. The primary

Bayley-II	Bayley Scales of Infant Development-Second Edition
CHD	Congenital heart disease
MDI	Mental developmental index
SES	Socioeconomic status
WPPSI-III	Wechsler Preschool and Primary Scale of Intelligence-III

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outcome was neurodevelopmental outcome. The Canton Zurich ethics committee approved the study.

Patients were recruited at the University Children's Hospital in Zurich prior to surgery. Parents were asked to participate in the study, and written informed consent was obtained. Follow-up assessment was performed at 1, 4, and 6 years of age at the Child Development Center outpatient clinic.

Of 211 eligible children, 16 died within the first year of life and, thus, 187 of 195 children (follow-up rate 96%) were assessed at 1 year of age. Two children died between the 1- and 4-year follow-ups. At 6 years of age, 166 children were seen (**Figure 1**; available at www.jpeds.com). Of those, 148 participated in 1-, 4- and 6-year assessment and, thus, 39 were excluded (2 died, 5 moved away, 15 refused, 17 other) because of missing follow-up after 1 year of age. Socioeconomic status (SES) was similar between excluded and included subjects (P = .079) Excluded subjects had smaller head circumference at birth (P = .008) and lower preoperative neurologic severity score (P = .036), fewer cyanotic heart defects (P = .008), were older at their first bypass surgery (P = .010), had higher weight at first surgery (P <.001), and shorter intensive care unit (P = .008) and hospital stay (P = .006) (**Table I**). The total number of children analyzed in this report was 148.

The 1-year assessment included the Bayley Scales of Infant Development-Second Edition (Bayley-II), which provides a mental developmental index (MDI).[11] At the 4- and 6-year follow-ups, 111 children were examined with the Wechsler Preschool and Primary Scale of Intelligence-III, and 37 were tested with a combination of the Wechsler Preschool and Primary Scale of Intelligence-IIII, the Snijders Omen Nonverbal Test of Intelligence, the Wechsler Intelligence Scale for Children Third Edition, or the Kaufman Assessment Battery for Children.[12-15]

At 1 year of age, motor function was assessed using the Bayley-II psychomotor developmental index. At 4 years of age, the Movement Assessment Battery for Children 2 was applied.[16] The test consists of 3 parts assessing manual dexterity, aiming and catching, and static and dynamic balance, which provide a composite score. At 6 years of age, the Zurich Neuromotor Assessment was applied.[17] The 4 motor components of the Zurich Neuromotor Assessment (pure motor function, adaptive fine motor function, adaptive gross motor function, and static balance) were averaged into a single total motor score.

Data on a large number of medical variables were collected from the patient's chart (for details see the study by Naef et al[18]). In addition, children underwent a neurologic examination prior to cardiac surgery. During neurologic examination, posture, movements, cranial nerves, tone, muscle reflexes, and adaptation/behavior were assessed and summarized in a neurologic severity score ranging from 0 to 18. Note that higher scores indicate worse neurologic status.[19] SES was estimated by means of a 6-point score of both maternal education and parental occupation. The lowest score is 2 (lowest

Table I. Subject and treatment characteristics

Characteristics	Valid data, incl/excl	Median (range); no. (%)		*P* value*
		Included n = 148	Excluded† n = 39	
Male sex	148/39	94 (63.5)	23 (59)	.602
Biventricular heart defect	148/39	118 (79.7)	36 (92.3)	.079
Cyanotic heart defect	148/39	102 (68.9)	18 (46.2)	.008
Prematurity <37 wk	147/38	15 (10.2)	3 (7.9)	.543
Gestational age	147/38	39.6 (30.6; 43.0)	39.7 (30.4; 41.7)	.789
SES	138/9	8 (2; 12)	7 (3; 10)	.079
5'Apgar	137/25	9 (1; 10)	9 (5; 10)	.703
Birth weight SDS	148/39	−0.06 (−5.4; 3.8)	−0.22 (−3.8; 3.6)	.867
Birth length SDS	145/35	−0.08 (−4.9; 4.2)	−0.46 (−4.1; 2.2)	.745
Head circumference SDS	128/22	−0.43 (−6.5; 2.9)	−0.76 (−4.2; 6.1)	.008
Preoperative neurologic severity score	111/18	2 (0; 11)	1.5 (0; 7)	.036
Preoperative feeding difficulties	148/38	33 (22.4)	5 (13.2)	.362
Age at first surgery, mo	148/39	1.92 (0.10; 24.16)	4.5 (0.1; 56.9)	.010
Weight at first surgery SDS	148/39	−0.20 (−1.26; 2.52)	0.77 (−0.83; 4.33)	<.001
ECC‡ time, min	148/39	155.5 (25; 405)	139 (40; 405)	.095
DHCA time, ‡ min§	6/2	30 (1; 145)	29.5 (27; 32)	1.00
Lowest temp, first surgery, °C	148/39	30 (16; 37)	32 (22; 37)	.065
Length of ICU stay, ‡d	148/39	7 (1; 232)	5 (2; 100)	.008
Length of hospital stay, ‡d	148/39	24 (8; 227)	17 (8; 284)	.006
Postoperative seizures	147/39	1 (0.6)	2 (5.1)	.127
Reoperation	148/39	47 (31.8)	3 (7.7)	.715
Cognitive function SDS 1 y	148/32	−0.53 (−1.07; −0.07)	−0.67 (−3.3; 1.1)	.533
Motor function SDS 1 y	148/29	−1.87 (−2.67; −1.20)	−1.5 (−3.9; 1.1)	.081

DHCA, deep hypothermic circulatory arrest; *ECC*, extracorporeal circulation time; *ICU*, intensive care unit.
*Pearson χ^2 for binomial variables and Mann-Whitney U test for continuous variables were applied.
†Missing follow-up after 1 year assessment.
‡At first surgery.
§DHCA in 28 subjects (26 included vs 2 excluded).

socioeconomic background), and the highest 12. For better illustration, SES was divided into 3 groups: lowest socioeconomic background: SES (2-5), medium SES (6-8), and highest socioeconomic background SES (9-12) in accordance with Largo et al.[20,21] The therapies children received any time until 6-year follow-up were assessed by means of questionnaires filled out by the parents at 4- and 6-year assessment and classified as cognitive intervention (early intervention and learning support) or motor intervention (physical and occupational therapy and psychomotor therapy), and speech and language therapy.

Cognitive and total motor score were adjusted for age and sex with respect to a population of typically developing children, as defined by the test instruments in use. All scores were expressed as SDS to provide an average of 0 and a SD of 1 for typically developing children, with higher scores indicating better performance. A SDS below −1 (corresponding to the 15th percentile of typically developing children) was considered as cognitive delay or motor function below average. For comparison between included and excluded subjects, a Pearson χ^2 test was applied for binomial data and a Mann-Whitney U test for continuous data.

To assess cohort stability of cognitive and motor function, we compared average scores obtained at 1-, 4-, and 6-year examinations against normative values and tested whether there was a significant improvement across the ages in cognitive and motor function. For this, a linear mixed model was fitted, with neurodevelopmental outcome (cognitive or motor) as the dependent variable, with age as an independent variable (fixed effect) and child as a random effect to take into account the fact that scores for the same child are not independent.

Further we tested, whether medical or demographic factors interacted significantly with cognitive or motor development. For this, a medical/demographic factor and the interaction of the medical/demographic factor with age were added to our linear mixed model. Each medical/demographic factor was examined separately in a univariate analysis. Medical/demographic factors were identified from the literature and included sex, gestational age, and growth measures at birth (weight, height and head circumference SDS), biventricular heart defect, preoperative neurologic severity score, number of bypass surgeries, preoperative feeding difficulties, age at first surgery, extracorporeal circulation time, deep hypothermia, SES, length of intensive care unit stay, and cognitive and motor therapies.[6,9,22] Linear mixed models were fitted using the lme routine from the nlme library (v 3.1) in the R statistical package (v 3.1.0; https://CRAN.R-project.org/package=nlme). SPSS 24.0 (IBM Corp, Armonk, New York) was used for group comparison in Table I.

To assess individual stability of cognitive and motor function, we calculated Spearman correlations between test scores obtained at 2 different ages. Correlations were compared using bootstrap. In addition, we calculated sensitivity, specificity, positive and negative predictive value, and ORs for 6-year cognitive impairment (defined as below −1 SDS) based on 1-year cognitive delay (below −1 SDS). Any P values of less than .05 were considered statistically significant.

Results

Median age in years was 1.0 (0.9- 2.5) at the age 1-year examination, 4.3 (3.9- 4.8) at the age 4-year examination, and 6.3 (5.5- 6.6) at the age 6-year examination. Details of demographic, medical variables of in- and excluded children are presented in Table I. A total of 118 (79.7%) children had a biventricular heart defect and 30 (20.3%) a univentricular CHD. Table II (available at www.jpeds.com) lists cardiac diagnoses. Fifteen (10.2%) children were born prematurely (<37 weeks, 1 child <32 weeks), and the number of bypass surgeries ranged from 1 to 4, with most children undergoing 1 (68.2%) or 2 (17.6%) bypass surgeries by the age of 6 years. Until the age 6-year assessment, 22 (14.9%) children received a cognitive intervention and 21 (14.9%) received a motor intervention. Another 21 (14.2%) children received speech and language therapy.

Cohort Stability

Boxplots for cognitive and motor development at age 1-, 4-, and 6-year examinations are provided in Figure 2 (mean and SD, Table III). Note that total motor score at the age of 4 years was higher than at the age of 6 years. All effects reported in our linear mixed models were largely similar with or without the inclusion of therapy as a cofactor.

Both cognitive and motor function of the total cohort mildly improved over time (cognitive: P = .01; motor: P <.001) (Figure 2). Concurrently, the percentages of children with a cognitive delay (MDI/IQ <85, ie, SDS< −1) decreased between age 1 and 6 years (28.4% at 1 year, 25.0% at 4 years, and 22.3% at 6 years). For motor function, the raw percentages of children with scores below −1 SDS were 78.4% at age 1 year, 14.3% at age 4 years, and 34.3% at age 6 years.

We found a significant interaction only for the factor SES (P <.001, + 0.033 SD in cognitive performance per SES point each year, corresponding to + 0.16 SD in cognitive performance per 1 SES point between 1 and 6 years of age). Figure 3 depicts this interaction; patients are divided into the 3 SES categories. Although the 3 groups had a similar performance at age 1 year, they diverged at older ages. The performance decreased with age in the low SES group, remained stable in the middle SES group, and increased with age in the high SES group (IQ difference between highest and lowest SES group: 1.14 SD = 17.1 IQ points at age 6 years).

We found significant interactions for 3 medical or demographic factors: SES (P = .001), weight at birth (P = .048), and head circumference at birth (P = .006). Figure 3 shows an illustration of the interaction of head circumference at birth with age (data not shown for the interaction of SES and birth weight). Patients are divided into 2 categories. Motor performance of the children below the 10th percentile with respect to either head circumference or

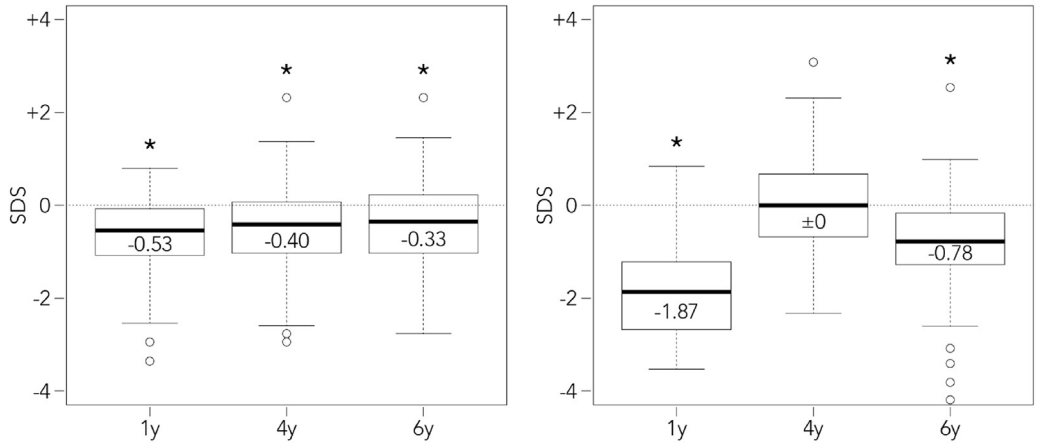

Figure 2. Total population cognitive and motor outcome at follow-up. Cognitive and motor outcome for the total population (N = 148) is presented as boxplots at 1, 4, and 6 years of age. The data is expressed as SDS (mean: 0, SD ± 1 in typically developing children). The upper/lower borders of the box are third/first quartile, respectively. The thick line in the box is the median. *Comparison with normative values: cognitive function: *P* values 1, 4, and 6 years <.001; motor function: *P* values 1 and 6 years <.001, 4 years = .503.

weight at birth was similar to those above or equal to the 10th percentile at the age of 1 year (all approximately 2 SDs below the norm), but the groups diverged afterward. Those children above or equal to the 10th percentile improved more than those children below the 10th percentile between the ages of 1 and 6 years.

Individual Stability

For cognitive function, correlation between age 1 and 4 years, between age 4 and 6 years, and between age 1 and 6 years was significant for all time intervals (1-4 years: rho = 0.24, 95% CI 0.08-0.39, $P = .003$, 4-6 years: rho = 0.56, 95% CI 0.43-0.67, $P < .001$, 1-6 years: rho = 0.20, 95% CI 0.04-0.34, $P = .016$). The correlation was higher for ages 4-6 years than for ages 1-4 years ($P = .001$), but did not differ between age 1 and 4 years and 1 and 6 years ($P = .59$).

For motor function, correlation was significant for all time intervals (1-4 years: rho = 0.25, 95% CI 0.07-0.42, $P = .005$; 4-6 years: rho = 0.50, 95% CI 0.35-0.63, $P < .001$, 1-6 years: rho = 0.23, 95% CI 0.06-0.38, $P = .006$). Again, the correlation was higher for ages 4-6 years than for ages 1-4 years ($P = .014$) but did not differ between age 1 and 4 years and 1 and 6 years ($P = .80$).

Table III. Neurodevelopmental outcome

Outcome measure	Mean (SD) N = 148
Cognitive function SDS	
1 y of age	−0.63 (0.79)
4 y of age	−0.47 (0.90)
6 y of age	−0.41 (0.91)
Motor function SDS	
1 y of age	−1.84 (1.06)
4 y of age	−0.03 (0.98)
6 y of age	−0.79 (1.00)

Correlation strengths for cognitive and motor function were similar at the time interval age 1-6 years of age ($P = .78$) and for 1-4 and 4-6 years of age (1-4 years: $P = .93$, 4-6 years: $P = .52$). Notably, they both showed higher correlation coefficients between 4 and 6 years of age than between 1 and 4 years of age. Figure 4 shows an illustration of correlation coefficients.

Because of the weak correlation between measurements at ages 1 and 6 years, the association of abnormal IQ (<-1 SDS) at age 6 years based on an abnormal cognition at age 1 year (MDI < −1 SDS) was not significant with an OR of 1.35 (95% CI 0.6-3.1; sensitivity 33.3%, specificity 73%; positive predictive value 26.2%; negative predictive value 79.2%). This is also reflected by the considerable number of children who changed category between the age 1- and 6-year assessment (they are represented by the dots in the top left and bottom right quadrant in Figure 4).

Discussion

Prediction of neurodevelopmental outcome in children at risk for impairments, such as children with CHD, is important for parental counseling, initiation of early interventions, and identification of modifiable risk factors. However, we have shown that individual neurodevelopmental stability is only moderate at best in our cohort of children with CHD. This makes the prediction of future outcome based on early neurodevelopmental assessments difficult; our study highlights the need for continued follow-up assessments as these children grow.

Analyzing cognitive and motor outcome from 1 to 6 years of age in a large prospective cohort of children with CHD who underwent cardiopulmonary bypass surgery enabled us to demonstrate that at a group level, cognitive abilities improved during this time period. This is consistent with

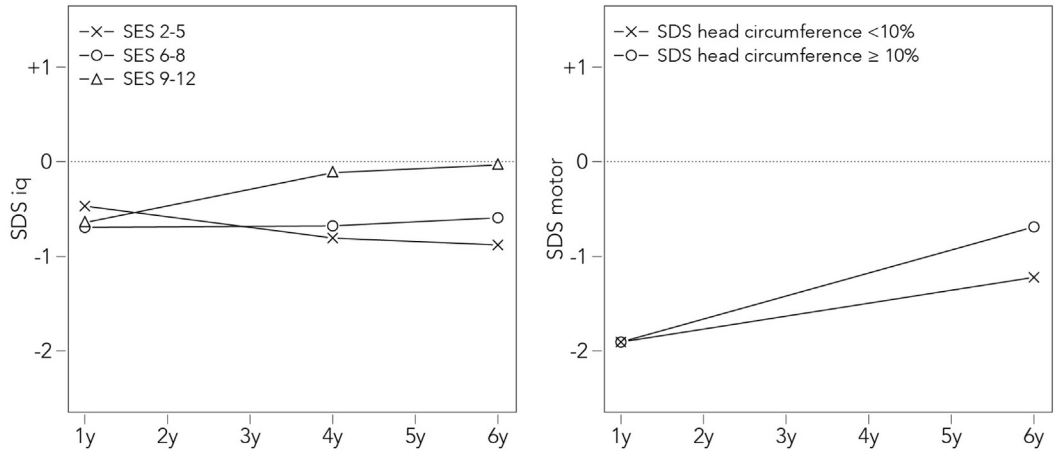

Figure 3. Interaction of socioeconomic status with cognitive development (*left panel*) and of head circumference at birth with motor development (*right panel*). To illustrate the significant interactions with raw data, cognitive functions at each age (1, 4, and 6 years) were averaged separately for the 3 SES categories: lowest 2-5, moderate 6-8 and highest 9-12 (*left panel*), and motor functions at 1 and 6 years were averaged separately for a head circumference above/equal and below the 10th percentile (data at age 4 years are not presented because of the test instrument effect, as explained in the Results section). SES interacted significantly with cognitive development (P = .001), and head circumference at birth interacted significantly with motor development (P = .006).

the finding of Sterken et al, which showed an improvement in both IQ scores and executive function between 4 and 7 years of age.[5] Furthermore, we observed an improvement in motor abilities, which is consistent with the findings of Mussatto et al.[4] Although motor function improved considerably, the improvement in cognitive functions was only small in our study, with 22.3% of children performing below −1 SDS in tests at the age of 6 years. This is in line with a study in adolescents with CHD in whom neurodevelopmental deficits remained.[2] Thus, children with CHD may not fully outgrow their cognitive difficulties.[2] Further, Calderon et al showed in a study of patients with CHD age 5-7 years that different neurodevelopmental domains differed in their developmental pattern, with both catch-up and persistence of neurodevelopmental delay.[23] Further follow-up into adulthood can determine whether children outgrow or grow into their difficulties.

When examining the interaction of various factors with age on cognitive and motor development, SES was the only one that showed an age-dependent effect on cognitive function. Cognitive performance improved most with age in those children with the highest SES. For motor function, higher SES, larger head circumference at birth, and higher weight at birth were associated with an improving performance across the ages. The influence of SES on neurodevelopment has previously been described in preterm children and in typically developing children, where the effect of SES varied among studies.[20,24]

Physicians should take the influence of SES into clinical consideration. Therapeutic and social support should be considered as early as possible, especially for children from lower socioeconomic backgrounds, even if neurodevelopmental impairments are mild because impairments will likely consolidate over time. Future studies are necessary to investigate the influence of SES as children reach adolescence and adulthood.

In our cohort, cardiac factors did not interact with neurodevelopment. This is in contrast to another study in patients with CHD. Hoffman et al found a negative impact of reintervention on cognitive development.[6,22] Their study investigated children between ages 1 and 3 years with repeated assessment using the Bayley-III. Repeated assessment during the first 3 years of life, when many reinterventions occur, may be more sensitive to alterations in neurodevelopment during this age-period,[6] whereas longer intervals and outcome assessment capture the long-term trend rather than fluctuations associated with acute interventions. Both are important for describing and helping to understand the mechanisms of changes in development and for counseling parents and healthcare professionals. The discrepancy in results may also be due to differences in cohorts. For instance, cognitive and motor development may be influenced by factors, such as resilience, neuroplasticity, therapeutic interventions, or adverse life events. Further studies are necessary to capture the effect of these factors. Of note, in our cohort the frequency of therapeutic interventions was rather low.

Our examination of individual cognitive stability showed that correlation between consecutive assessments was only weak to moderate for both cognitive and motor outcome. Thus, prediction of IQ in childhood based on early developmental assessment is limited. This limitation is well described for other at-risk populations, such as those born extremely preterm.[8,22,25] As a consequence, children who develop deficits later may be missed and may not receive appropriate therapeutic support, and others may be over treated if later cognitive performance is predicted solely

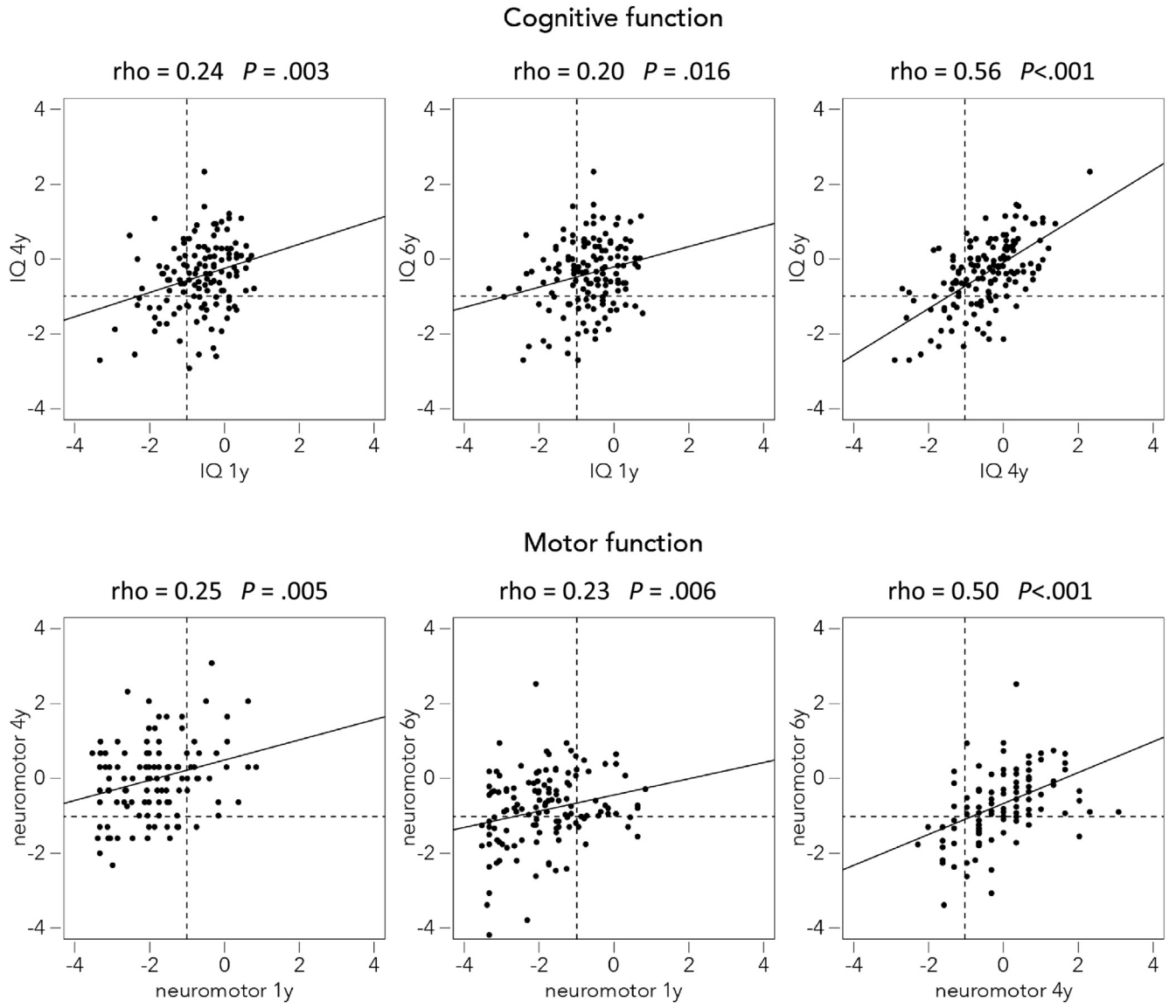

Figure 4. Individual stability of neurodevelopmental measures. Correlation and corresponding *P* values for cognition and motor function are presented for the time intervals 1-4, 1-6, and 4-6 years. All correlations presented were significant ($P < .05$). The horizontal and vertical dashed lines indicate the cut-off at −1 SDS and define 4 quadrants. Children with an instable neurodevelopmental performance (changing from above/equal to below −1 SDS and vice versa) are in the top left and bottom right quadrant.

by the 1-year neurodevelopmental examination. It is, therefore, important to provide ongoing neurodevelopmental surveillance in children with CHD to ensure optimal therapeutic support.

Although individual cognitive and motor stability was only weak to moderate, it increased as children grew older. Individual correlations between 1 and 4 years of age were smaller than between 4 and 6 years of age. Although this may partially be accounted for by the different time spans, it seems conceivable that correlations between consecutive tests increase as children grow older. Thus, it is likely that the prediction of a future outcome based on a past outcome will become more accurate at older ages. Although the increase in correlation strength may partially be attributed to the same test battery applied for cognitive testing at 4 and 6 years of age, the same does not apply for motor testing, where different test tools were applied at 4 and 6 years of age. Both cognitive and motor functions showed similar correlation coefficients for corresponding time intervals.

When comparing individual stability (correlation strengths) in our population of patients with CHD to a study examining the role of early developmental assessment for later outcome in healthy and preterm-born children, individual stability was similar.[20] However, the same study found a higher individual stability in children with impaired cognitive function (IQ <85) compared with our cohort (CHD: 1-6 years: rho = 0.20, 95% CI 0.04-0.34; children with IQ <85: 9 months-7 years: rho = 0.4-0.6).[20] In addition, studies

examining children with developmental disabilities or cognitive delay suggest that lower cognitive performance is associated with higher individual cognitive stability.[20,26-28]

The current study has some limitations. We only included patients who were able to complete follow-up at 1, 4, and 6 years of age. Children with significant neurodevelopmental disabilities are less likely to have completed follow-up assessment, and, thus, the improvement of neurodevelopment in our population may be overestimated. This is particularly true for children with a genetic diagnosis who are more likely to have neurodevelopmental disabilities. As we have excluded these children, our findings can only be generalized to the population of patients with CHD without a genetic diagnosis. To assess neurodevelopment, age-appropriate assessment tools were applied that differed at 1, 4 and 6 years of age. Thus, some variation in test results may be attributed to the different test tools applied. Also, the neuropsychologist performing the neurodevelopmental assessment was not blinded to the medical history and neurodevelopmental findings at previous ages.

For the individual child, prediction of neurodevelopmental outcome based on early assessments remains difficult. Repeated follow-up assessments are essential to ensure optimal therapeutic support and to minimize over- and under treatment. ■

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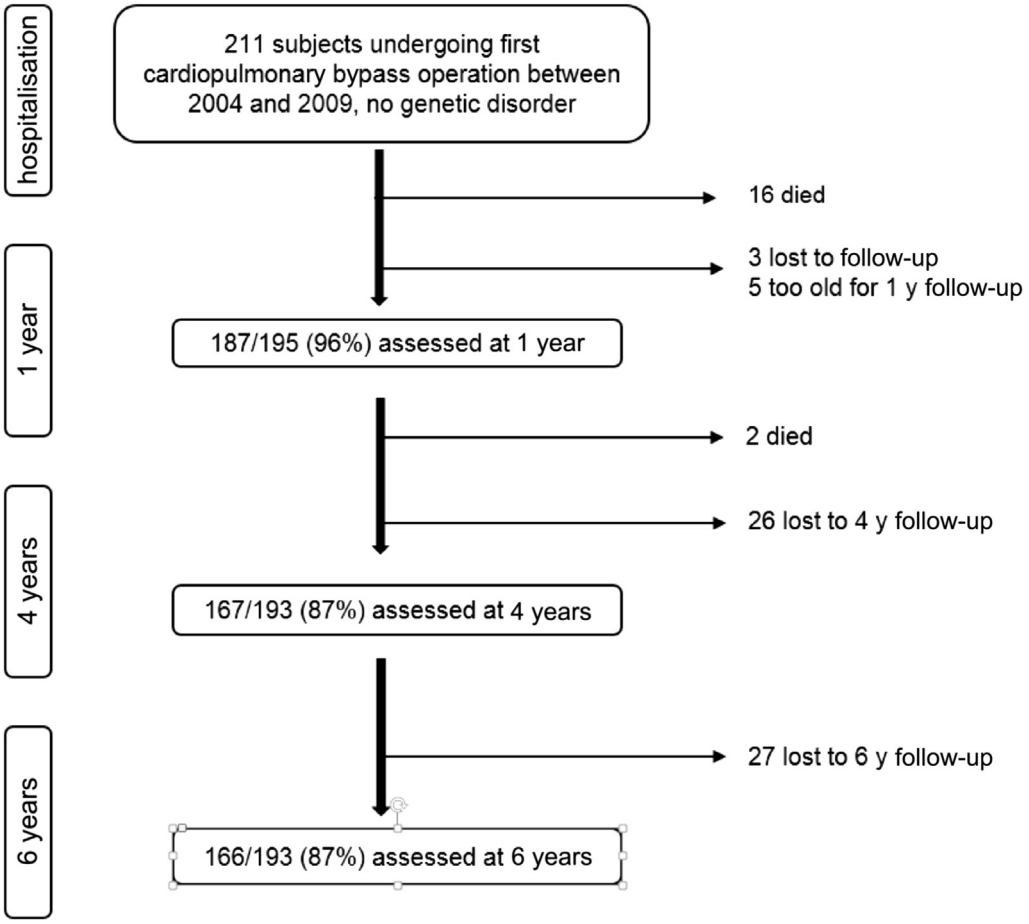

Figure 1. Flow sheet.

Table II. Cardiac diagnoses

Two-ventricle congenital heart defects	**118 (79.7%)**
Transposition of the great arteries with intact ventricular septum	23 (15.5%)
Ventricular septal defect without interrupted aortic arch	21 (14.1%)
Double inlet left ventricle with ventricular septal defect	19 (12.8%)
Tetralogy of Fallot	15 (10.1%)
Atrioventricular canal defect	7 (4.7%)
Coarctation/arch hypoplasia	7 (4.7%)
Truncus arteriosus	6 (4.1%)
Total anomalous pulmonary venous connection	5 (3.4%)
Tetralogy of Fallot with pulmonary atresia	2 (1.4%)
Atrial septal defect sinus venosus	2 (1.4%)
Anomalous left coronary artery from the pulmonary artery	2 (1.4%)
Pulmonary valve stenosis	2 (1.4%)
Aortic valve stenosis	2 (1.4%)
Ventricular septal defect with interrupted aortic arch	1 (0.7%)
Double outlet right ventricle Fallot type	1 (0.7%)
Hemitruncus	1 (0.7%)
Atrial septal defect II	1 (0.7%)
Pulmonary atresia/intact ventricular septum	1 (0.8%)
Single-ventricle congenital heart defects	**30 (20.3%)**
Double inlet left ventricle	8 (5.4%)
Hypoplastic left heart syndrome	7 (4.7%)
Pulmonary atresia with ventricular septal defect, main aortopulmonary collateral artery	3 (2.0%)
Pulmonary atresia/intact ventricular septum	2 (1.4%)
Double outlet right ventricle	2 (1.4%)
Tricuspid atresia	1 (0.7%)
Ebstein anomaly and pulmonary stenosis	1 (0.7%)
Crisscross heart	1 (0.7%)
Double outlet right ventricle with transposition of the great arteries	1 (0.7%)
Functional single ventricle	1 (0.7%)
Heterotaxie	1 (0.7%)
Atrioventricular septal defect, pulmonary atresia, intact ventricular septum, total anomalous pulmonary venous connection	1 (0.7%)
Unbalanced atrioventricular septal defect, hypoplastic right ventricle	1 (0.7%)

An overview is presented of cardiac diagnosis of all children included in this report (n = 148). A total of 104 (70.3%) children had a biventricular defect without arch obstruction and 14 (9.5%) with arch obstruction. In children with a univentricular defect, 14 (6.5%) had a defect without arch obstruction and 16 (10.8%) with arch obstruction.