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Language development in children with congenital heart disease aged 12–24 months

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ABSTRACT

This longitudinal study aims to describe the trajectory of language development in children with CHD aged 12–24 months assessed through an early monitoring and individualized intervention program. We also sought to determine whether early language performances, at 12 months of age, predict 24-month language abilities.

We conducted developmental assessments of 49 children with CHD using the Bayley Scales of Infant and Toddler Developmental, third edition (Bayley-III) at 12 and 24 months, and the MacArthur-Bates Communicative Development Inventories (MBCDI) at 12, 18 and 24 months.

Compared to normative populations, CHD patients showed significantly lower mean scores in both receptive and expressive language scales of the Bayley-III and the MBCDI at 12 months, whereas at 18 and 24 months only expressive language scores were reduced. No differences were found in the cognitive scale. Communicative gestures at 12 months were significantly predictive of language skills at 24 months of age.

Our findings indicate specific vulnerability of language outcome, especially in expressive skills, rather than a global cognitive impairment in our patients with CHD. We recommend using communicative gestures as an early marker of language development to improve our ability to detect language delays in this population.

Abbreviations: CHD, congenital heart disease; Bayley-III, Bayley Scales of Infant and Toddler Development, Third Edition; MBCDI, MacArthur-Bates Communicative Development Inventories; PICU, pediatric intensive care unit.

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1. Introduction

Children with congenital heart disease (CHD) requiring cardiac surgery are known to be at higher risk of neurodevelopmental delays in speech and language acquisition.[1–8] A large proportion of these children experience delayed onset of language, as well as impaired pronunciation, and require speech or language therapy.[1,9] At 15 months of age, children with CHD obtain lower scores (on average 10 to 17 points lower) on standardized language assessments for both expressive and receptive skills compared to healthy children, with more significant impairments in expressive compared to receptive skills.[10,11] At 21 months of age, the language impairment rate of 15.5% largely exceed normative expectations, whereas rates of cognitive impairments remain in the normal range (≤2.27%).[11] Speech and language delays seem to persist, as the proportion of children showing abnormal language development generally increases with age. At 24 months, more than 25% of children with CHD manifest lower communicative skills.[12,13] At school-age, children with CHD often exhibit lower phonologic awareness skills, poorer expressive and receptive vocabulary, impaired strategies for lexical access and difficulties in spelling and reading.[4,14] These impairments have been shown to be strongly associated with behavioral problems and reduced school achievements.[15]

Given the prevalence of neurodevelopmental delays in children with CHD, the American Heart Association and the American Academy of Pediatrics recommended systematic developmental monitoring from the age of 9 months to improve the early detection and the therapy offered in the case of impairment.[16] At our cardiac neurodevelopmental clinic, our program of early surveillance and intervention consists of extensive developmental assessments at 4, 8, 12, 18 months, and older. Additional therapy is offered, in the form of educational support and interventional sessions, based on the child's needs and the family concerns.

Although speech and language delays have previously been reported in children with CHD, no longitudinal study has investigated the earliest language abilities in this population. Using a longitudinal design, the present study aims to describe the trajectory of language development in children with CHD aged 12–24 months enrolled in an early and systematic monitoring and individualized intervention program. As language impairments are typically detected at preschool or school age, where they may have an impact on academic achievements, it is of utmost importance to improve our ability to detect the earliest indices of atypical language development. Therefore, we also sought to determine the association between early language performances and future language abilities, in order to refine monitoring procedures in young children with CHD.

2. Method

2.1. Participants and procedure

We recruited 49 infants with CHD (23 females, 26 males) who underwent cardiac surgery. All participants are patients followed at the *Clinique d'Investigation Neuro-Cardiaque* (CINC) of the Sainte-Justine University Hospital Centre. All children had normal hearing ability as determined by hearing screening test. We excluded patients with a genetic syndrome known to impact neurodevelopment (e.g. trisomy 21 or 22q11 deletion spectrum) and those exposed to more than one language at home[17] – remaining participants were exclusively French-speaking. As part of their clinical follow-up, participants were submitted to language assessments either by formal examination or parental questionnaires at 12, 18 and 24 months (±1 month), which correspond to the timings of our clinical follow-ups. At 12 and 24 months, cognitive and language development were assessed using the Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III). At 12, 18 and 24 months of age, parents filled out the MacArthur-Bates Communicative Development Inventories (MBCDI).[18] Our clinical protocol implies that patients performing at or under the 10th percentile rank on all scales of the MBCDI or equal, or under the 2nd percentile rank on one scale are considered at high risk of language delay and are referred to additional language assessment performed by a speech therapist. The Bayley-III allows to obtain a general picture of the child's neurodevelopment, which complements the specific language assessment.

Perinatal (gestational age, birth weight, Apgar score at 5 min, prenatal diagnosis), surgical (cardiopulmonary bypass time, cross clamp time), postsurgical (pediatric intensive care unit [PICU] length stay, hospital length stay) and demographic factors (sex and maternal education level) were collected from medical records. Cyanotic heart defects were defined as defects resulting in arterial blood desaturation from the bypassing of deoxygenated blood into the systemic circulation or the mixture of oxygenated and deoxygenated blood entering the systemic circulation.[19] Anatomic CHD classification were extracted from cardiac diagnosis according to Clancy et al. as following: Class I, two-ventricle heart without arch obstruction; Class II, two-ventricle heart with arch obstruction; Class III, single-ventricle heart without arch obstruction; Class IV, single-ventricle heart with arch obstruction.[20] Surgical risk category were extracted according to Jenkins et al.[21] from the description of surgical procedures.

This study was approved by the Research Ethics Board of the Sainte-Justine University Hospital Centre, and all families provided written informed consent for participating in the study.

2.2. Language assessment tools

The Bayley-III[22] is a multidisciplinary battery assessing several developmental domains, including cognitive and language development, in infants aged 1–42 months. The Cognitive scale estimates sensorimotor development, objects exploration, and concepts formation, and the Global Language scale measures receptive skills, such as receptive vocabulary and morphological comprehension, and expressive skills, such as preverbal communication and morphosyntactic development. Raw scores can be converted into standard scores and percentile ranks for the Cognitive and the Global Language scales, and into standard scores for the Receptive and Expressive Language scales. Scores of 1–2 standard

deviations below average suggest mild delays, scores of 2–3 standard deviations below average reflect moderate delays, and scores greater than 3 standard deviations below average suggest severe delays.[23]

The MBCDI[20] are age-specific parental questionnaires measuring communicative abilities in children aged 8–30 months. Parents are asked to identify whether their child understands or produces various words, sentences, and communicative gestures, and to rate the complexity of the child's productions. The *Words and Gestures* inventory, intended for 8- to 16-month-old infants, is divided into four scales: Word Comprehension, Sentence Comprehension, Word Production, and Communicative Gestures. Intended for 16- to 30-month-old infants, the *Words and Sentences* inventory is also divided into four scales of expressive language skills: Expressive Vocabulary, Sentence Complexity, Mean Length of Utterance, and Grammatical Forms. For each scale, raw scores can be converted into percentile ranks. In the present study, we used the Quebec French adaptation which has been standardized on a normative sample of 1363 French-speaking children.[18]

2.3. Statistical analyses

Descriptive statistics were used to characterize clinical, sociodemographic and developmental data of our patient group. Independent sample t-tests were applied to test whether the cognitive and language scores assessed with the Bayley-III and MBCDI were similar to a normative population. Several analyses were conducted to compare cognitive and language development and to characterize developmental trajectory of language abilities. First, we performed two repeated measures ANOVA on Bayley-III Global Language and Cognitive, and Receptive and Expressive Language scores with the age (12 vs. 24 months) and the developmental sphere (cognitive vs. language and receptive vs. expressive) as within subject factors. We then performed repeated measures ANOVA on MBCDI expressive vocabulary scores (Word Production at 12 months and Expressive Vocabulary at 18 and 24 months). We only used the expressive vocabulary scales of the MBCDI since it is the only recurrent scale at all ages. Greenhouse-Geisser adjustment for violation of sphericity was conducted when necessary. Pairwise comparisons were carried out to identify significant differences and corrections for multiple comparisons were performed using Bonferroni's procedure.

Pearson bivariate correlations were conducted between demographic variables, clinical factors, 12- and 24-months language scores. Multiple regressions were then performed to assess the value of 12-month language performance in predicting 24-months language skills. Language scores at 24 months were used in the regression model as dependent variables. Clinical and demographic variables known to influence language development (i.e. birth weight and maternal education level)[2–4,24] and 12-months scores significantly correlated with 24-months scores were used as independent variables.

Assumptions needed to perform parametric tests were verified and satisfied, and no multicollinearity were found among the independent variables included in multiple regression models. Significance level was set at $p < 0.05$. Statistical analyses were performed using SPSS version 25.0 (IBM Corp. Armonk, NY).

3. Results

3.1. Characteristics of the patients

Participants' demographic and clinical characteristics are reported in Table 1. The most common heart defects were transpositions of the great arteries, tetralogy of Fallot, ventricular septal defect, coarctation of the aorta, and double outlet right ventricle. There was no significant difference in maternal education level, anatomic CHD classification, and surgical risk category between our study group and the whole cohort of children with CHD followed-up at the CINC, suggesting that our sample is representative of the population of children followed at the clinic.

3.2. Language outcome and trajectory between 12 and 24 months

MBCDI and Bayley-III scores, and percentage of infants considered at risk of language delays are presented in Table 2. At 12 months, our study group performed significantly lower on both receptive and expressive scales, compared to normative samples (Bayley-III Receptive Language: t [143] = 3.40; $p < 0.001$; Bayley-III Expressive Language: t [143] = 2.49; $p = 0.014$; MBCDI Word Production: t [104] = 2.56; $p = 0.012$). They showed lower expressive language skills at 18 (MBCDI Expressive Vocabulary: t [93] = 3.; $p < 0.001$) and 24 months (Bayley-III Expressive Language: t [138] = 2.29; $p = 0.023$; MBCDI Expressive Vocabulary: t [97] = 3.59; $p < 0.001$: MBCDI Grammatical Form: t [93] = 3.52; $p < 0.001$; MBCDI Sentence Complexity: t [96] = 3.61; $p < 0.001$; MBCDI Mean Length of Utterances: t [96] = 4.19; $p < 0.001$), whereas no difference was found for receptive scores at 24 months. No differences with the normative sample were found with respect to cognitive outcomes at 12 and 24 months of age.

Results revealed that our patient group showed significantly lower Global Language performance compared to Cognitive scale (F [1] = 37.183, $p < 0.001$, $\eta_p^2 = 0.522$) at both 12 (difference of 8 points on composite scores; $p < 0.001$) and 24 months (difference of 5 points on composite scores; $p < 0.001$). We also found a significant interaction between age and language sphere (F [1] = 12.718, $p = 0.001$, $\eta_p^2 = 0.256$), with a significant increase of Receptive Language performances from 12 to 24 months ($p = 0.014$), but no change in Expressive Language scores. At 12 months, our study group performed significantly lower in Receptive compared to Expressive Language scale ($p = 0.019$), whereas Expressive tend to be lower to Receptive Language scores at 24 months ($p = 0.060$). Finally, we found no significant effect of age on MBCDI scores (F [1551] = 0.791, $p = 0.431$, $\eta_p^2 = 0.030$).

3.3. Prediction of 24-months language skills

We found small correlations of gestational age and birth weight with both 12- and 24-months Bayley-III language scores (gestational age: $r = 0.324–0.364$; $p < 0.05$; birth weight:

Table 1 – Participants characteristics.

	n (%)	Mean (SD)	Range
Total	49 (100)	–	–
Male	26 (53)	–	–
Prenatal diagnosis	26 (53)	–	–
Gestational age at birth (weeks)	49 (100)	38.42 (2.0.7)	30.71–41.14
Birth weight (kg)	49 (100)	3.10 (0.58)	0.98–4.11
APGAR score at 5 min	47 (96)	8.79 (0.91)	6–10
Type of cardiac lesion[50]			
Cyanotic lesion	29 (59.2)	–	–
Acyanotic lesion	20 (40.8)	–	–
Anatomic CHD classification[20]			
Class I	35 (71.4)	–	–
Class II	9 (18.4)	–	–
Class III	2 (4.1)	–	–
Class IV	3 (6.1)	–	–
Maternal education level	45 (92)	–	–
High school	13 (28.9)	–	–
Vocational school	13 (28.9)	–	–
College/university	19 (42.2)	–	–
Primary surgery			
Age at surgery (days)	49 (100)	100.9 (137.5)	3–578
Cardiopulmonary bypass time (min)	46 (94)	127.39 (94.69)	0–410
Cross clamp time (min)	46 (94)	79.80 (52.59)	0–200
PICU length stay (days)	49 (100)	11.43 (14.96)	1–77
Hospital length stay (days)	49 (100)	26.71 (35.96)	4234
Second surgery required	4 (8.2)	–	–
Surgical risk categories[21]			
Category 2	24 (48.9)	–	–
Category 3	17 (34.7)	–	–
Category 4	6 (12.3)	–	–
Category 6	2 (4.1)	–	–
Developmental follow-up			
Age at 12-month assessment (months)	45 (91.8)	12.27 (0.42)	11.31–13.48
Age at 12-month questionnaire (months)	34 (69.4)	11.99 (0.55)	10.32–13.48
Age at 18-month questionnaire (months)	41 (82)	17.97 (0.88)	17.00–21.83
Age at 24-month assessment (months)	41 (83.7)	24.64 (0.60)	23.83–26.40
Age at 24-month questionnaire (months)	46 (93.8)	23.96 (0.62)	21.66–25.44

SD, standard deviation; n, number of participants; CHD, congenital heart disease; PICU, pediatric intensive care unit.

$r = 0.295–0.353$; $p < 0.05$). MBCDI Communicative Gesture scores at 12 months were significantly correlated with all MBCDI and Bayley-III scores at 24 months ($r = 0.462–0.628$; all $p < 0.01$). MBCDI Sentence Comprehension performances at 12 months were also significantly associated with several language scores at 24 months ($r = 0.0385–0.467$; $p < 0.05$). Details of correlations are presented in Table 3. Overall, regression analyses confirmed these findings wherein communicative gestures at 12 months of age was a strong predictor of both receptive and expressive language skills at 24 months. We found no predictive effect of birth weight and maternal education on 24-month language abilities. Regression analyses results are detailed in Table 4.

4. Discussion

This study aimed to characterize language development of children with CHD between 12 and 24 months who participated in an early and systematic monitoring and intervention program of the cardiac neurodevelopmental clinic at the Sainte-Justine University Hospital Centre.

4.1. *Language outcome and trajectory*

The standardized language assessments and parental reports evaluations revealed reduced language skills in our patient group compared to normative data in both receptive and expressive domains – although remaining within the average –, whereas no differences were found with respect to intellectual outcome. Furthermore, our study group exhibited lower language performances compared to their intellectual functioning, with the average language composite scores of 9 and 8 points below the cognitive scores at 12 and 24 months, respectively. Our data are in accordance with the previous reports of a dissociation between the intellectual and language outcome at 21 months of age, with CHD children showing on average language composite scores of 5 points below the cognitive scores of the Bayley-III.[1] At this age, the rate of cognitive impairments remains within the normative expectation whereas the rate of language impairments is seven times higher.[11] Thus, in agreement with previously documented observations, our findings do not suggest a global developmental delay in children with CHD, but rather a specific vulnerability for language development. Although our

Table 2 – Mean standard scores, mean and median percentile ranks, number and percentage of participants performing 1 and 2 SD below average at each time-point.

	Mean SS (SD)	Mean PR (SD)	Median PR	n ≤ −1 SD (%)	n ≤ −2 SD (%)
12 months					
Bayley-III Cog	98.90 (9.65)	48.00 (18.88)	50.00	2 (4.88)	1 (2.44)
Bayley-III GL	90.36 (15.52)	33.24 (21.34)	34.00	8 (17.78)	3 (6.67)
Bayley-III RL	8.36 (1.81)	31.36 (20.52)	38.00	13 (28.89)	0 (0.00)
Bayley-III EL	8.73 (2.43)	35.64 (27.49)	38.00	8 (17.78)	2 (4.88)
MBCDI WP	–	32.80 (26.88)	25.00	14 (42.42)	0 (0.00)
MBCDI CG	–	40.34 (33.83)	28.00	11 (37.50)	4 (12.50)
MBCDI SCompr	–	40.44 (29.97)	39.00	8 (25.00)	5 (15.62)
MBCDI RV	–	37.50 (32.39)	28.50	13 (38.23)	4 (11.76)
18 months					
MBCDI EV	–	27.41 (25.58)	20.00	20 (48.78)	2 (4.88)
MBCDI GF	–	37.65 (28.08)	22.00	1 (3.85)	0 (0.00)
MBCDI MLU	–	38.91 (25.30)	24.00	8 (19.51)	1 (2.44)
MBCDI SCompl	–	41.47 (16.33)	38.00	0 (0.00)	0 (0.00)
24 months					
Bayley-III Cog	99.65 (12.22)	49.02 (25.03)	50.00	7 (15.91)	1 (2.27)
Bayley-III GL	94.65 (13.60)	37.97 (24.24)	34.00	6 (17.64)	1 (2.94)
Bayley-III RL	9.35 (2.57)	42.63 (29.10)	38.00	8 (20.00)	1 (2.5)
Bayley-III EL	8.78 (2.49)	36.12 (28.17)	38.00	13 (32.5)	1 (2.5)
MBCDI EV	–	27.08 (28.44)	14.00	23 (51.11)	6 (13.33)
MBCDI GF	–	26.37 (30.22)	8.00	23 (56.10)	7 (17.07)
MBCDI MLU	–	25.32 (21.34)	20.00	17 (38.66)	1 (2.27)
MBCDI SCompl	–	28.27 (23.09)	19.25	21 (46.73)	0 (0.00)

SS, standard scores; PR, percentile ranks; SD, standard deviation; n, number of participants; Cog, Cognitive; GL, Global Language; RL, Receptive Language; EL, Expressive Language; WP, Word Production; CG, Communicative Gestures; SCompr, Sentence Comprehension; RV, Receptive Vocabulary; EV, Expressive Vocabulary; GF, Grammatical Form; MLU, Mean Length of Utterance; SCompl, Sentence Complexity.

results concur with the observations that children with CHD are at higher risk of neurodevelopmental delays of language functioning,[1–5,25,26] this is the first study to document such a discrepancy between language and intellectual functioning as early as 12 months of age.

Neurodevelopmental disorders in CHD were shown to arise from a complex interaction between the genetic, environmental risk factors and brain alterations occurring both before and after birth.[27] In recent years, a growing literature has identified a high prevalence of delayed brain development and white matter injury in fetuses and infants with CHD[28–32] – remarkably similar to those observed in preterm infants.[33,34] For example, Clouchoux and associates revealed, during the mid-to-late gestation in CHD fetuses compared to controls, a delayed sulcation of the anterior ascendant ramus,[32] typically located within the speech production areas, as well as a more shallow posterior regions of the superior temporal sulcus, the latter being involved in speech comprehension. Interestingly, the delayed structural and microstructural brain development was associated with an impaired brain functioning in neonates and adolescents with CHD.[35–38] Hence, we believe that the delayed development in both the frontal and temporal cortical areas, starting *in utero*, combined with pre- and postnatal white matter alterations, may lead to specific language impairments. It would be interesting to further investigate the patterns and value of early connectivity alterations in predicting language and cognitive impairments in infants and children with CHD.

Our patient group showed lower expressive compared to receptive language skills at 24 months of age. This is in line

Table 3 – Pearson bivariate correlation matrix between language scores.

12-months *scores*		24-months scores						
		MBCDI EV	MBCDI GF	MBCDI MLU	MBCDI SCompl	Bayley-III GL	Bayley-III RL	Bayley-III EL
MBCDI SCompr	*r*	0.422[a]	0.385[a]	0.467[b]	0.434[a]	0.382	0.389	0.329
MBCDI RV	*r*	0.226	0.108	0.412[a]	0.303	0.309	0.284	0.297
Bayley-III RL	*r*	0.267	0.249	0.346[a]	0.272	0.458[b]	0.386[a]	0.464[b]
MBCDI EV	*r*	0.272	0.447[a]	0.419[a]	0.294	0.266	0.198	0.305
Bayley-III EL	*r*	0.317[a]	0.429[a]	0.463[a]	0.421[a]	0.529[a]	0.378[a]	0.605[a]
MBCDI CG	*r*	0.547[b]	0.487[b]	0.628[b]	0.524[b]	0.539[b]	0.550[b]	0.462[a]

SCompr, Sentence Comprehension; RV, Receptive Vocabulary; EV, Expressive Vocabulary; EL Expressive Language; CG, Communicative Gestures; GF, Grammatical Form; MLU, Mean Length of Utterance; SCompl, Sentence Complexity; GL, Global Language; RL, Receptive Language.
[a] $p \leq 0.05$.
[b] $p \leq 0.01$.

Table 4 – Results of multiple regression analyses between 12- and 24-months language scores.

Regression models		24-months scores					
		MBCDI EV	MBCDI GF	MBCDI MLU	MBCDI SCompl	Bayley-III EL	Bayley-III RL
1. Birth weight	β	0.151	0.130	0.064	0.222	0.043	−0.046
Maternal education	β	0.025	−0.002	−0.019	0.028	0.151	−0.007
MBCDI CG	β	0.529[a]	0.479[a]	0.617[b]	0.473[a]	0.507[a]	0.680[b]
	R^2	0.256	0.139	0.311	0.231	0.232	0.352
2. Birth weight	β	0.215	0.159	0.080	0.223	0.105	0.043
Maternal education	β	0.174	0.177	0.201	0.196	0.386	0.304
MBCDI SCompr	β	0.365	0.368	0.470[a]	0.403[a]	0.314	0.378
	R^2	0.138	0.066	0.192	0.195	0.099	0.074
3. Birth weight	β	0.220	0.092	0.151	0.274	0.013	0.024
Maternal education	β	0.221	0.109	0.203	0.205	0.329	0.249
MBCDI EV	β	0.273	0.491[a]	0.413[a]	0.287	0.512[a]	0.292
	R^2	0.078	0.177	0.153	0.110	0.278	0.013
4. Birth weight	β	0.200	0.245	0.025	0.273	0.168	0.024
Maternal education	β	0.144	0.065	0.128	0.151	0.254	0.069
Bayley-III RL	β	0.173	0.191	0.344	0.166	0.446[b]	0.334
	R^2	0.035	0.007	0.076	0.077	0.235	0.028
5. Birth weight	β	0.209	0.249	0.031	0.256	0.115	0.013
Maternal education	β	0.129	0.021	0.083	0.105	0.237	0.062
Bayley-III EL	β	0.148	0.323	0.347	0.249	0.512[b]	0.258
	R^2	0.026	0.079	0.071	0.107	0.294	−0.023

SCompr, Sentence Comprehension; EV, Expressive Vocabulary; CG, Communicative Gestures; GF, Grammatical Form; MLU, Mean Length of Utterance; SCompl, Sentence Complexity; RL, Receptive Language; EL, Expressive Language.

[a] $p \leq 0.05$.

[b] $p \leq 0.01$.

with what was documented by Hallioglu and colleagues (2015) at 15 months[10] and by Acton and colleagues (2001) at 21 months.[11] Expressive language skills, further than receptive, are thus at particular risk in children with CHD. These impairments were shown to persist, particularly in pragmatics, which represents interactive language skills. Indeed, children with CHD aged 4 and 8 years old produce less symbolic talk during playtime and fewer narrative components compared to typically developing children.[6,39,40]

Although we found no significant effect of age on MBCDI Expressive Vocabulary scores, our study group seemed to exhibit decreasing performances on all MBCDI scales at 24 months, as illustrated by low average means and median scores, and slightly higher proportions of children performing under the clinical cut-offs at this age. Results also revealed increasing Bayley-III Receptive Language performances, despite no change in Expressive Language scores from 12 to 24 months of age. Altogether, these observations arise questions regarding the developmental trajectory of language impairments. Indeed, literature on neurodevelopment of children with CHD suggest that subtle or mild delays may increase with age[6,41] and difficulties may accelerate with environmental demands. While children may exhibit a nearly normal acquisition of early language milestones, difficulties may emerge later during development, which could lead to persistent impairments. For instance, it has been reported that a late word combination was a stronger risk factor of language disorder than a late onset of word production.[42] Hence, development of language skills in children with CHD should be monitored to identify whether language delay progresses into a language disorder or whether children will catch up with their same-age peers.

Whereas the current data do not allow us to assess the effect of our early and systematic surveillance and individualized intervention program, neurodevelopmental trajectory of our patient group may have been influenced by interventions.[43] Although all children benefited from indirect intervention through educational support and recommendations of activities and exercises to parents, a few of them received additional care regarding language development. While we observed similar language performances compared to studies using Bayley-III during the first two years of life in children with CHD,[10,11] our study group exhibit higher intellectual functioning. This discrepancy may reflect the beneficial effect of early and systematic multidisciplinary surveillance in this population. On the other hand, we could not exclude that the most severe cardiac lesions such as univentricular heart defects may be underrepresented in our patient group, leading to a potential overestimation of intellectual functioning. Further investigation is still needed to characterize language development in larger samples and investigate the potential benefits of our early surveillance and individualized intervention program.

4.2. *Prediction of 24-months language skills*

We also aimed at determining the association between 12- and 24-month language abilities, and clinical and demographic factors. We found no predictive effect of birth weight and maternal education, but we showed that communicative gestures at 12 months is a strong predictor of both receptive and expressive language skills at 24 months. Communicative gestures refer to the non-verbal behaviors being used for the purpose of intentional communication.

They usually emerge between 7 and 12 months in typically developing infants and represent a way to interact with others and communicate information before infants are able to speak. For example, at 12 months, we expect infants to be able to reach out to give an object, holding arms out to be picked up, or participate in game routines such as peek-a-boo or patty-cake.[18] Several studies conducted in typically developing or very preterm children revealed that gesture inventory appears to be an important predictor of later expressive vocabulary and overall language abilities.[44–46] In infants with CHD, we observe a late onset of these behaviors as well as reduced inventory and frequency of gestures, that probably reflect the specific vulnerability of language development. On the other hand, it is not to be excluded that the prevalent motor delays observed in infants with CHD may affect the emergence of communicative gestures, as demonstrated in infants at risk of developmental disorder.[47,48] It would be interesting to investigate in future studies the specific association between motor development and emergence of communicative gestures in infants with CHD.

Regarding the clinical practice, our findings raise the question of which criteria should be used to recommend further language assessment. Despite good psychometric properties of the MBCDI,[18] the way each scale represents best the child's global language development may change across ages due to developmental variability. The Expressive Vocabulary scale at 12 months, and the Sentence Complexity and the Grammatical Forms scales at 18 months may be less representative of the child's global language skills since at this age these abilities initiate their development. This variability should thus be considered in the interpretation of language performances and clinicians should give prominence to the most representative scales for age (i.e. gesture at 12 months and expressive vocabulary at 18 months). As a consequence of these implications and our findings, criteria at our cardiac neurodevelopmental clinic have been revised to place greater emphasis on communicative gesture. Children performing below the 10th percentile rank on the MBCDI Communicative Gestures scale were thereby considered at high risk of language delay and were subsequently referred to language assessment with a speech therapist. In this regard, clue analysis of the progress of these interventions will be reported in later publications.

4.3. *Limitations of the current research*

As participants have different language profiles, they did not have access to the same intervention modality or frequency of interventions which could have influenced the language trajectory of our patient group. Furthermore, as developmental assessments were performed in a clinical context, some children may have missed assessments at some time points, which accounts in part for the missing data and may lead to a small sample size. Nevertheless, this study allows to characterize early language development in our patient group and brings very interesting thoughts to refine our strategies of early detection of language delays. In addition, specific limits exist regarding the Bayley-III Language scale. The protocol is not validated in French, which could complicate the administration of language concepts that do not have French-equivalents (e.g. verbs ending in –ing). However, this does not concern any item at 12 months and at most 5 items of the receptive scale and 4 items of the expressive scale at 24 months. Aware of this limitation, at our cardiac neurodevelopmental clinic we decided to systematically administer these items according to the French version of the Preschool Language Scale, 4th Edition,[49] from which the Bayley-III language items were inspired,[22] insuring reliable within- and between-individuals comparisons. In addition, the Bayley-III is less sensitive to measure language content since higher scores are acquired as soon as a few words are listed. This has already been described in children with CHD where the Bayley-III tends to overestimate the child's abilities, leading to a potential under-identification of developmental delays.[11,23] However, we believe that combining different tools (i.e. formal assessment and questionnaires) and several sources of information (i.e. clinician and parents) is a strength of the study and it heightens reliable results and increases the sensitivity and the specificity of the developmental assessments.

5. Conclusions

In summary, our study revealed lower language performance compared to normative populations in our patient group of infants with CHD aged 12–24 months, in both the receptive and expressive domains. Furthermore, the impairment preferentially affects expressive skills. Therefore, language development in this population requires close follow-up to ensure that mild delays do not progress into significant troubles with growing environmental demands, and that language skills catch up those of typically developing children. Accordingly, we intend to follow our cohort to assess increasingly complex language skills such as pragmatics, phonological awareness, lexical access, and narration, as well as the potential impact of these complex skills on academic achievements. As documented in typically developing children, our results also highlight communicative gesture at 12 months of age as an early predictive marker of both receptive and expressive skills at 24 months. Hence, we advocate for closer surveillance of communicative gestures to more efficiently identify young children at high risk of language delay.

Conflict of interest

None.

Acknowledgments

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REFERENCES

1. Hövels-Gürich H, Bauer SB, Schnitker R, Hinckeldey KW, Messmer BJ, Seghaye M-C. Long-term outcome of speech and language in children after corrective surgery for cyanotic or acyanotic cardiac defects in infancy 2008;**12**:378–86.
2. Limperopoulos C, Majnemer A, Shevell MI, Rohlicek C, Rosenblatt B, Tchervenkov C, Darwish HZ. Predictors of developmental disabilities after open heart surgery in young children with congenital heart defects. *J Pediatr* 2002;**141**:51–8.
3. Majnemer A, Limperopoulos C, Shevell M, Rohlicek C, Rosenblatt B, Tchervenkov C. Developmental and functional outcomes at school entry in children with congenital heart defects. *J Pediatr* 2008;**153**(1):55–60.
4. Miatton M, De Wolf D, François K, Thiery E, Vingerhoets G. Neuropsychological performance in school-aged children with surgically corrected congenital heart disease. *J Pediatr* 2007;**151**:73–8.
5. Gaynor JW, Stopp C, Wypij D, Andropoulos DB, Atallah J. Neurodevelopmental outcomes after cardiac surgery in infancy 2015;**135**(5).
6. Bellinger DC, Newburger JW. Neuropsychological, psychosocial, and quality-of-life outcomes in children and adolescents with congenital heart disease. *Prog Pediatr Cardiol* 2010;**29**(2):87–92.
7. Fourdain S, Vanasse C-M, Poirier N, Carmant L, Gallagher A. Cardiopathies congénitales : physiopathologie, facteurs de risque et profils neuropsychologiques. *Rev Quebecoise Psychol* 2016;**37**(2):1–18.
8. Nattel SN, Adrianzen L, Kessler EC, Andelfinger G, Dehaes M, Côté-Corriveau G, Trelles MP. Congenital heart disease and neurodevelopment: clinical manifestations, genetics, mechanisms, and implications. *Can J Cardiol* 2017;**33**:1543–55.
9. Calderon J, Bonnet D, Pinabiaux C, Jambaqué I, Angeard N. Use of early remedial services in children with transposition of the great arteries. *J Pediatr* 2013;**163**:1105–10.
10. Hallioglu O, Gurer G, Bozlu G, Karpuz D, Makharoblidze K, Okuyaz C. Evaluation of neurodevelopment using bayley-III in children with cyanotic or hemodynamically impaired congenital heart disease. *Congenit Heart Dis* 2015;**10**(6):537–41.
11. Acton BV, Biggs WSG, Creighton DE, Penner K a H, Switzer HN, Thomas JHP, Joffe AR, Robertson CMT. Overestimating neurodevelopment using the bayley-III after early complex cardiac surgery. *Pediatrics* 2011;**128**(4):794–e800.
12. Sananes R, Manlhiot C, Kelly E, Hornberger LK, Williams WG, Macgregor D, Buncic R, Mccrindle BW. Neurodevelopmental outcomes after open heart operations before 3 Months of age. *Ann Thorac Surg* 2012;**93**(5):1577–83.
13. Bricker D, Squires J, Moutns L, Potter L, Nickel R, Twombly E, Farrell J. *Ages and Stages Questionnaires: a parent-completed, child-monitoring system*. 2nd ed., vol. 3. Child and Family Services Update; 2004.
14. Wray J, Sensky T. *Congenital heart disease and cardiac surgery in childhood : effects on cognitive function and academic ability*. 2001. p. 687–91.
15. Hövels-gürich HH, Konrad K, Wiesner M, Minkenberg R, Herpertz-Dahlmann B, Messmer BJ, von Bernuth G. Long term behavioural outcome after neonatal arterial switch operation for transposition of the great arteries. *Arch Dis Child* 2002;**87**:506–11.
16. Marino BS, Lipkin PH, Newburger JW, Peacock G, Gerdes M, Gaynor JW, Mussatto KA, Uzark K, Goldberg CS, Johnson WH, Li J, Smith SE, Bellinger DC, Mahle WT. Neurodevelopmental outcomes in children with congenital heart Disease : evaluation and management: a scientific statement from the American heart association. *Circulation* 2012;**126**:1143–72.
17. Paradis J. Bilingual children's acquisition of English verb morphology: effects of language exposure, structure complexity, and task type. *Lang Learn* 2010;**60**(3):651–80.
18. Trudeau N. *Les Inventaires MacArthur-Bates du développement de la communication (IMBCD)*. 2008.
19. Brickner ME, Hillis LD, Lange RA. Medical progress second of two parts. *N Engl J Med* 2000;**342**(5):334–42.
20. Clancy RR, Mcgaurn SA, Wernovsky G, Spray TL, Norwood WI, Jacobs ML, Murphy JD, Gaynor JW, Goin JE. Preoperative risk-of-death prediction model in heart surgery with deep hypothermic circulatory arrest in the neonate. *J Thorac Cardiovasc Surg* 2000;**119**(2):347–57.
21. Jenkins KJ, Gauvreau K. Center-specific differences in mortality: preliminary analyses using the risk adjustment in congenital heart surgery (RACHS-1) method. *J Thorac Cardiovasc Surg* 2002;**124**(1):97–104.
22. Bayley N. *Bayley scales of infant and toddler development*. 3rd ed. San Antonio, TX: Pearson; 2006.
23. Long SH, Galea MP, Eldridge BJ, Harris SR. *Performance of 2-year-old children after early surgery for congenital heart disease on the Bayley Scales of Infant and Toddler Development*. 3rd ed., vol. 88. Early Human Development; 2012. p. 603–7.
24. Bellinger DC, Wypij D, Rappaport LA, Jonas RA, Wernovsky G, Newburger JW. Neurodevelopmental status at eight years in children with dextro-transposition of the great arteries: the Boston Circulatory Arrest Trial 2003;**126**(5):11–3.
25. Tomblin B, Records NL, Buckhwalter P, Zhang X, Smith E, Marlea O. Prevalence of specific language impairment in kindergarten children. *JSLHR (J Speech Lang Hear Res)* 1997;**40**(6):1245–60.
26. Association AP. In: *Diagnostic and statistical manual of mental disorders: DSM-IV-TR. American P*. Washington, DC: American Psychiatric Association; 2000.
27. Wernovsky G, Licht DJ. Neurodevelopmental outcomes in children with congenital heart disease-what can we impact? *Pediatr Crit Care Med* 2016;**17**(8):232–42.
28. Licht DJ, Shera DM, Clancy RR, Wernovsky G, Montenegro LM, Nicolson SC, Zimmerman R a, Spray TL, Gaynor JW, Vossough A. Brain maturation is delayed in infants with complex congenital heart defects. *J Thorac Cardiovasc Surg* 2009;**137**(3):529–36. Discussion 536–7.
29. Miller SP, McQuillen PS, Hamrick S, Xu D, Glidden DV, Charlton N, Karl T, Azakie A, Ferriero DM, Barkovich AJ, Vigneron DB. Abnormal brain development in newborns with congenital heart disease. *N Engl J Med* 2007;**357**:1928–38.
30. Limperopoulos C, Tworetzky W, McElhinney DB, Newburger JW, Brown DW, Robertson RL, Guizard N, McGrath E, Geva J, Annese D, Dunbar-Masterson C, Trainor B, Laussen PC, Du Plessis AJ. Brain volume and metabolism in fetuses with congenital heart disease: evaluation with quantitative magnetic resonance imaging and spectroscopy. *Circulation* 2010;**121**(1):26–33.
31. Brossard-Racine M, Du Plessis AJ, Vezina G, Robertson R, Bulas D, Evangelou IE, Donofrio M, Freeman D, Limperopoulos C. Prevalence and spectrum of in utero structural brain abnormalities in fetuses with complex congenital heart disease. *Am J Neuroradiol* 2014;**35**(8):1593–9.
32. Clouchoux C, Plessis AJ, Bouyssi-Kober M, Tworetzky W, McElhinney DB, Brown DW, Gholipour A, Kudelski D, Carfield SK, McCarter RJ, Robertson Jr RL, Evans AC, Newburger JW, Limperopoulos C. Delayed cortical

development in fetuses with complex congenital heart disease. *Cerebr Cortex* 2013;**23**:2932–43.
33. Miller SP, McQuillen PS. Neurology of congenital heart disease: insight from brain imaging. *Arch Dis Child Fetal Neonatal Ed* 2007;**92**(6):435–7.
34. Volpe JJ. Encephalopathy of congenital heart disease-destructive and developmental effects intertwined. *J Pediatr* 2014;**164**:962–5.
35. Birca A, Vakorin VA, Porayette P, Madathil S, Chau V, Seed M, Doesburg SM, Blaser S, Nita DA, Sharma R, Duerden EG, Hickey EJ, Miller SP, Hahn CD. Interplay of brain structure and function in neonatal congenital heart disease. *Ann Clin Transl Neurol* 2016;**3**(9):708–22.
36. De Asis-Cruz J, Bouyssi-Kobar M, Evangelou I, Vezina G, Limperopoulos C. Functional properties of resting state networks in healthy full-term newborns. *Sci Rep* 2015;**5**:17755.
37. Panigrahy A, Schmithorst VJ, Wisnowski JL, Watson CG, Bellinger DC, Newburger JW, Rivkin MJ. Relationship of white matter network topology and cognitive outcome in adolescents with d-transposition of the great arteries. *Neuroimage: Clin.* 2015;**7**:438–48.
38. Rollins CK, Watson CG, Asaro LA, Wypij D, Vajapeyam S, Bellinger DC, DeMaso DR, Robertson Jr RL, Newburger JW, Rivkin MJ. White matter microstructure and cognition in adolescents with congenital heart disease. *J Pediatr* 2014;**165**(5):936–44.
39. Ovadia R, Hemphill L, Winner K, Bellinger D. Just pretend: participation in symbolic talk by children with histories of early corrective heart surgery. *Appl Psycholinguist* 2000;**21**(3):321–40.
40. Hemphill L, Uccelli P, Winner K, Chang C, Bellinger D. Narrative discourse in young children with histories of early corrective heart surgery. *J Speech Lang Hear Res* 2002;**3**(45):318–31.
41. Hövels-Gürich HH, Seghaye MC, Schnitker R, Wiesner M, Huber W, Minkenberg R, Kotlarek F, Messmer BJ, Von Bernuth G. Long-term neurodevelopmental outcomes in school-aged children after neonatal arterial switch operation. *J Thorac Cardiovasc Surg* 2002;**124**(3):448–58.
42. Rudolph JM, Leonard LB. early language milestones and specific language impairment. *J Early Interv* 2016;**38**(1):41–58.
43. Gallagher A, Dagenais L, Doussau A, Décarie J-C, Materassi M, Gagnon K, Prud'homme J, Vobecky S, Poirier N, Carmant L. Significant motor improvement in an infant with congenital heart disease and a rolandic stroke: the impact of early intervention. *Dev Neurorehabil* 2017;**20**(3):165–8.
44. Rowe ML, Goldin-Meadow S. Early gesture selectively predicts later language learning. *Dev Sci* 2009;**12**(1):182–7.
45. Iverson JM, Goldin-Meadow S. Gesture paves the way for language development. *Psychol Sci* 2005;**16**:367–71.
46. Suttora C, Salerni N. Gestural development and its relation to language acquisition in very preterm children. *Infant Behav Dev* 2012;**35**:429–38.
47. Lebarton ES, Iverson JM. Associations between gross motor and communicative development in at-risk infants. *Infant Behav Dev* 2016;**44**:59–67.
48. Benassi E, Savini S, Iverson JM, Guarini A, Caselli MC, Alessandroni R, Faldella G, Sansavini A. Early communicative behaviors and their relationship to motor skills in extremely preterm infants. *Res Dev Disabil* 2016;**48**:132–44.
49. Zimmerman I, Steiner V, Pond R. *Preschool Language scale*. 4th ed. San Antonio, TX: The Psychological Corporation; 2002.
50. Hoffman JIE, Kaplan S. The incidence of congenital heart disease. *J Am Coll Cardiol* 2002;**39**(12):1890–900.