Intelligence and Hypoxemia in Children With Congenital Heart Disease: Fact or Artifact?

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Previous studies have reported lower intelligence for cyanotic than for acyanotic children with congenital heart disorders, a finding attributed to the degree of hypoxemia present. Several important variables have not been examined consistently, however, including coexisting neurologic or genetic disorders, definitive surgery, degree of sickness, age at testing, sex and social class. The present study examined the relation of these variables to obtained intelligence measures for 82 consecutively admitted children, excluding children with abnormal neurologic examinations and those having received definitive surgery. Consistent with earlier reports, intelligence quotients for the acyanotic children (112.81 ± 14.52 mean ± SD) were significantly higher (t = 2.60; p = 0.006) than for the cyanotic group (103.50 ± 15.81). Although sex, race and social class were not significantly different between the 28 cyanotic and the 54 acyanotic children, the cyanotic children were significantly sicker (χ^2 = 9.12; p = 0.005) and younger (t = 4.10; p = 0.001). However, when young and old children and the degree of sickness within cyanotic and acyanotic groups were compared, no significant differences were found. These findings demonstrate that intelligence differences between cyanotic and acyanotic children persist when the effect of neurologic abnormalities and definitive surgery is removed and remain despite the severity of sickness or child's age at testing.

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In the past several years, reparative surgery for congenital heart disorders has been instituted in patients at increasingly early ages. This practice, made possible by improved surgical techniques, has been based in large part on several studies (1,2) reporting lower intelligence for cyanotic than for acyanotic children, a finding attributed to the cumulative effect of long-standing hypoxemia on cognitive development. Among the several studies documenting lower intelligence for cyanotic than for acyanotic children, several potentially confounding variables have not been controlled consistently, including 1) coexistence of neurologic or genetic disorders, or both; 2) performance of definitive surgery; 3) severity of the child's illness at the time of intelligence testing; 4) social class of the child; 5) age at testing; and 6) instrument used to measure intelligence.

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Most studies addressing intelligence among children with congenital heart disorders have excluded children with obvious neurologic disorders or known genetic syndromes involving mental retardation (3–5); few, however, have directly evaluated the neurologic and genetic status of the patients included in the study (1,6–8). Thus, it is quite likely that children with subtle neurologic problems or nonidentified syndromes may have been included in these previous studies.

Another factor obscuring results has been the time of intelligence testing relative to definitive surgery. Some studies (4,5,8) have evaluated subjects before definitive surgery, others (1–3), after surgical repair; still other studies (7,8) have included subjects with and without definitive heart repair. Evaluating children after definitive surgery introduces the problem of the effect of surgical events on cognitive development. The assessment of development both before and after surgery for the same group of subjects is a rare design even for recent studies (9,10) investigating the effects of cardiac surgery with or without hypothermia on intellectual development. The majority of these reports (11–16) rely on postoperative evaluation with no preoperative evaluation of cognitive development. Consequently, the developmental delays identified in children after definitive sur-

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gery may well have antedated surgery and cannot be attributed summarily to surgical events. Studying intelligence in a surgically heterogeneous group does not permit the effects of cyanotic heart disease to be distinguished from those of surgery. In addition, most studies have not documented how sick a child was at the time of testing, even though children with congestive heart failure are known to perform more poorly than their well peers on a range of tasks. Many studies (6,9,10,12,13,16,17) also have failed to control for socioeconomic status.

Finally, the age range at which children have been tested presents a major confounding variable because the same intelligence tests cannot be used with all age groups and different tests measure different abilities. Thus, when comparing younger with older subjects, the intelligence quotients compared are typically derived from different intelligence tests (3,4,5,9).

The main objective of the present study was to determine whether the intelligence quotient differences favoring acyanotic children over cyanotic children are maintained among neurologically and genetically normal children tested before corrective surgery, when the factors of social class, sickness, age and intelligence test type are evaluated.

Methods

Patient selection. Before cardiac catheterization, all patients examined in the Division of Pediatric Cardiology at Rainbow Babies and Childrens Hospital from October 1981 through September 1983 were seen for a neurologic examination by a pediatric neurologist (M.W.L.) and for developmental assessment including intelligence testing (B.L.E.). Of the consecutive patients evaluated, 146 presented no neurologic, genetic or other congenital abnormalities in the neurologic examination. Other than the congenital heart disorders, all had a negative history by chart review and parental questionnaire for pre-, peri- and postnatal complications such as prematurity, asphyxia, neonatal syphilis, tracheostomy and maternal drug addiction. Eighty-two of the 146 neurologically normal patients had not received definitive surgery and served as subjects in the present study.

Demographic characteristics. The ages of these 82 neurologically normal subjects ranged from 0.25 to 15.92 years (mean ± SD 5.56 ± 4.44); 47 were boys and 35 were girls. All children were from monolingual English-speaking homes, with 67 white, 13 black and 2 Oriental children represented. Social class status was determined by the Hollingshead index of social position using employment as the determining factor. Children receiving a Hollingshead index of 1 and 2 were classified as having high, 3, 4 and 5 as mid and 6 and 7 as low social status.

Patient classification. Children with an arterial oxygen saturation level higher than 92% were classified as acyanotic, between 92 and 70% as mild to moderately cyanotic and 69% or less as severely cyanotic. Because of the small number of severely cyanotic children examined, all children with an oxygen saturation level of 92% or less were classified into one cyanotic group for statistical analysis. Subjects were classified on the basis of their clinical and cardiac catheterization data into two major categories of sickness: 1) Nonsick subjects in whom the severity of their heart disease and general state of health should not have interfered with their test performance. This group included 42 acyanotic and 13 cyanotic children; 2) Sick patients in whom the degree of congestive heart failure, severity of chronic cyanosis, cyanotic spells and general state of health would be expected to interfere with their test performance (12 acyanotic and 14 cyanotic children). One child could not be classified because of missing data. These classifications were performed by a pediatric cardiologist (G.B-S.) who was uninformed as to the intelligence test findings.

Measures. Each subject was administered an intelligence measure according to age. Subjects 2 months to 2.5 years were administered the Bayley Scales of Infant Development—Mental Scales; 2.5 to 4 years, the McCarthy Scales of Children's Abilities; 4 to 6.5 years, the Wechsler Preschool and Primary Scale of Intelligence (WPPSI) and 6.5 to 15 years, the Wechsler Intelligence Scale for Children–Revised (WISC-R). Subjects were tested by the same examiner and, whenever possible, testing was administered early in the morning the day before catheterization and before other laboratory measures were obtained.

Statistical analysis. Chi-square analysis was used to determine differences in sex, race and socioeconomic status between the cyanotic and acyanotic subjects. Age and intelligence quotient differences were tested using the t test except when the number of subjects in one group was less than 10, in which case a Mann-Whitney U test was employed. Differences among the intelligence quotients obtained through use of the four intelligence tests were assessed using a one-way analysis of variance.

A one-tailed test of probability was used when the difference between groups on a variable was expected to fall in a particular direction before the analysis. This procedure was applied when comparing 1) cyanotic with acyanotic subjects on intelligence test performance and degree of sickness, because cyanotic subjects were expected to do more poorly on these measures; and 2) sick with well subjects on intelligence test performance for the cyanotic and acyanotic groups separately and combined, because it was anticipated that the well subjects would perform best. For all other analyses, a two-tailed test of probability was used. Data are expressed as mean values ± SD.

Results

Clinical characteristics. The sex, race, social class, severity of sickness, mean age and mean intelligence quotients of the cyanotic and acyanotic groups are given in Table 1. Chi-square analysis revealed no significant differences for the cyanotic and acyanotic groups in sex, racial composition or social class. Although no significant difference between groups in socioeconomic status emerged, 11 of 54 subjects in the acyanotic group were of high socioeconomic status compared with only 2 of the 28 cyanotic children. It is possible that this nonsignificant difference between groups for social class had an effect on the outcome of testing in favor of the acyanotic group. As expected, significantly more cyanotic than acyanotic children were classified as sick (χ^2 = 9.12; p = 0.005). Age also differed between the groups, the cyanotic group representing significantly younger children than the acyanotic group (t = 4.10, p = 0.001).

Intelligence quotient. The Full Scale intelligence quotients for cyanotic and acyanotic children revealed that both groups were within the normal range (mean intelligence quotient 103.50 ± 15.81 in the cyanotic group and 112.81 ± 14.52 in the acyanotic group). The mean intelligence quotient for the acyanotic group, however, was significantly higher than that of the cyanotic group (t = 2.60; p = 0.006).

Age. The finding of a significantly lower intelligence quotient in cyanotic than in acyanotic subjects is consistent with earlier reports, but might have been affected by the significant age difference between the groups. Therefore, the relation between age and intelligence was examined.

Table 1. Cyanotic and Acyanotic Demographic Variables and Intelligence Quotient in 82 Subjects

	Cyanotic (n = 28)	Acyanotic (n = 54)	Value	Probability
Sex				
Male	17	30	χ^2 = 0.05	0.832
Female	11	24		
Race				
White	24	43	χ^2 = 1.19	0.553
Black	4	9		
Oriental	0	2		
SES				
High	2	11	χ^2 = 2.50	0.286
Mid	14	26		
Low	9	13		
Missing	3	4		
Sick				
Not sick	13	42	χ^2 = 9.12	0.005*
Sick	14	12		
Missing	1	0		
Age (yr)				
Mean	2.64	6.35	t = 4.10	0.001
SD	3.38	4.72		
IQ				
Mean	103.50	112.81	t = 2.60	0.006*
SD	15.81	14.52		

*One-tailed test of probability. IQ = intelligence quotient; SES = socioeconomic status.

First, intelligence quotient was compared in young (≤2.5 years) cyanotic (103.65 ± 16.57) and acyanotic (114.00 ± 17.63) children and in older (>2.5 years) cyanotic (103.13 ± 14.81) and acyanotic (112.68 ± 13.30) children. Again, even when the groups were more homogeneous in age, significant differences in intelligence favoring the acyanotic children emerged (Table 2).

Second, because the intelligence measures used were age-dependent, the question of variability in intelligence quotient obtained by the four intelligence tests was examined using a one-way analysis of variance. The mean intelligence quotient for the Bayley test, used with children 2.5 years and younger, was 108.41 (±17.61); for the McCarthy Scales, used with the 2.5 to 4 year old group, 112.57 (±11.80); the Wechsler Preschool and Primary Scale of Intelligence, for the 4 to 6.5 year olds, 115.25 (±16.41) and the Wechsler Intelligence Scale for Children–Revised, with children 6.5 years and older, 108.97 (±13.46). Analysis of variance results revealed no significant difference among these four intelligence measures (f = 0.52; p = 0.67).

A final age-related issue concerned within-group differences as the children get older. Specifically, do older cyanotic children perform more poorly than younger cyanotic children because they have had a longer period of hypoxemia? The results revealed almost identical values for intelligence quotient in young (103.65 ± 16.57) and older (103.13 ± 14.81) groups of cyanotic subjects. In addition, no difference was found between the young (114.00 ± 17.63) and old (112.27 ± 13.09) acyanotic groups. Overall, the obtained intelligence score was not related to age when this was examined for the entire group of children with congenital heart disorders within the cyanotic or acyanotic group or as a function of the intelligence test used.

Degree of sickness. Because significantly more cyanotic than acyanotic children were classified as sick, the possibility existed that sickness rather than cyanosis was the determining variable for cognitive level. Therefore, the relation between sickness and intelligence was evaluated (Table 2). When all well children were compared with all sick children without reference to oxygen saturation level, no significant difference was found between intelligence quotient in the well children (110.40 ± 14.37) and that in the sick children (107.73 ± 18.09). In examining cognitive level by state of health within the cyanotic group, no significant difference was found between intelligence quotient in sick cyanotic children (103.57 ± 15.06) and that in well cyanotic children (102.38 ± 17.33). Similarly, no difference was apparent between intelligence quotient in sick acyanotic children (112.58 ± 20.70) and that in well acyanotic children (112.88 ± 12.55). However, there was a significant difference between values in cyanotic (102.38 ± 17.33) and acyanotic (112.88 ± 12.55) children who were well (t = 2.03; p = 0.030). The difference between values in cyanotic (103.57 ± 15.06) and acyanotic (112.58

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Table 2. Relation of Age and Sickness to Intelligence Quotient in 82 Subjects

	No.	Mean IQ	SD	Value	Probability
Age					
Young					
Acyanotic	17	114.00	17.63	$t = 1.84$	0.038*
Cyanotic	20	103.65	16.57		
Old					
Acyanotic	37	112.68	13.30	U = 92.5	0.049*
Cyanotic	8	103.13	14.81		
Cyanotic					
Young	20	103.65	16.57	U = 76.5	0.858
Old	8	103.13	14.81		
Acyanotic					
Young	17	114.00	17.63	$t = 0.36$	0.722
Old	37	112.27	13.09		
Sickness					
All					
Well	55	110.40	14.37	$t = 0.66$	0.512
Sick	26	107.73	18.09		
Cyanotic					
Well	13	102.38	17.33	$t = 0.19$	0.425*
Sick	14	103.57	15.06		
Acyanotic					
Well	42	112.88	12.55	$t = 0.05$	0.481*
Sick	12	112.58	20.70		
Sick					
Acyanotic	12	112.58	20.70	$t = 1.25$	0.113*
Cyanotic	14	103.57	15.06		
Well					
Acyanotic	42	112.88	12.55	$t = 2.03$	0.030*
Cyanotic	13	102.38	17.33		

*One-tailed test of probability. IQ = intelligence quotient.

± 20.70) children who were sick approached but did not reach significance ($t = 1.25$; $p = 0.113$). In both situations, the cyanotic children, whether sick or well, did more poorly than the acyanotic children. Consequently, the degree of cyanosis again emerged as the factor most critically related to obtained cognitive level.

Discussion

The present study examined the intelligence of a carefully selected group of children with congenital heart disorders that included only children who were tested before definitive surgery and presented normal neurologic and genetic status by examination and history. Even with these strict subject criteria required for participation in the study, significant differences in intelligence quotient persisted favoring acyanotic over cyanotic children. Consequently, our overall findings are in agreement with data from earlier studies (3–6,8) in which subject selection criteria were less clearly defined or carefully controlled.

Demographic findings. Factors other than hypoxemia that could affect the difference in scores between the cyanotic and acyanotic groups were evaluated. Sex and race were comparable for the two groups and therefore could not explain the intelligence quotient differences. Social class was statistically comparable for cyanotic and acyanotic groups; however, only 7% of the cyanotic compared with 20% of the acyanotic children were from the high social classes. Thus, this disproportionately high number of acyanotic children from the high social classes may be a factor contributing to this group's higher obtained intelligence quotient.

Age and intelligence test variables. The cyanotic group was significantly younger than the acyanotic group. This difference may be attributed to the fact that children with cyanotic heart disease typically are operated on at a very early age, and only children who had not yet undergone definitive surgery were included in our study. The range of ages represented by the children in this study necessitated the use of different age-dependent cognitive tests, each composed of different tasks. Thus, it is conceivable that the cyanotic children obtained lower intelligence quotients because the majority were young and were administered one test, the Bayley Scales. However, no differences in obtained intelligence quotient were found among the four tests. Furthermore, when young cyanotic children were compared with young acyanotic children, all of whom had received the same test, the former group again were found to have a significantly lower intelligence quotient. These differences between cyanotic and acyanotic subjects persisted when the intelligence quotients obtained using the remaining three cognitive tests were compared in the older children. Finally, when comparing younger with older cyanotic children, no significant difference was found in intelligence scores. A similar finding resulted when comparing younger with older acyanotic children. Consequently, it appears that cyanosis and not the age at testing or the intelligence measure administered affects the intelligence score.

Degree of sickness. Other investigators have speculated that it is the degree of inactivity rather than hypoxemia that determines scores on intelligence tests, notably performance scores. Rasof et al. (5) and Silbert et al. (8) suggested that the lower activity levels and greater motor restrictions of the cyanotic children may have caused them to do more poorly on intelligence tests because they had less opportunity to explore their physical environment during infancy. Silbert et al. (8) subdivided their cyanotic and acyanotic groups into active and inactive groups. They found that the cyanotic children, whether active or inactive, continued to differ from the acyanotic children on intelligence scores. Unfortunately, their study did not discuss the criteria used to assign a subject to active or inactive status. In our study children were classified into a well group and a sick group, the latter including those subjects who had congestive heart failure and severe cyanotic spells or chronic cyanosis, or both. As expected, significantly more cyanotic than acyanotic children were classified as sick. These findings mirror those of Silbert et al. (8) in that, sick or well, cyanotic and acyanotic children continued to show a difference in intelligence score.

Practical importance of findings. Although this difference in intelligence quotient favoring acyanotic children was statistically significant, its practical importance may be less significant. Both groups achieved a mean intelligence quotient within the normal range, that of the cyanotic group falling comfortably within the average range and that of the acyanotic group within the high average (bright) range (18). Thus, the fact that the group mean for the cyanotic children remained in the normal range and was only slightly lower than that in the acyanotic children may be of more consequence than the statistical difference. The majority of children in both groups would be expected to function normally in a regular classroom. However, given their lower intelligence quotient, cyanotic children would be expected to be at a mild disadvantage compared with acyanotic children in academic achievement. Furthermore, a proportionately greater number of cyanotic than acyanotic children would be expected to have an intelligence quotient of less than 85, the lowest limit of the normal range.

Conclusions. Our findings demonstrate that the variables of neurologic and genetic status, definitive surgery, social class, age, intelligence test used and degree of sickness cannot explain the significantly lower intelligence scores obtained for cyanotic than for acyanotic children. It appears that the intelligence quotient results are not attributable to artifacts related to testing but may well be a fact of cyanotic heart disease.

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