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Neurodevelopment of Infants with Single-Suture Craniosynostosis: Presurgery Comparisons with Case-Matched Controls

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Abstract

Background—The hypothesized association between single-suture craniosynostosis and neurodevelopment remains unclear, given the methodologic limitations of previous studies, most notably the absence of control groups.

Methods—Standardized measures were used to assess the neurodevelopment of 125 matched case-control pairs shortly after cases were first diagnosed with isolated fusions of the sagittal, metopic, lambdoid, or right or left coronal sutures. Participants varied in age from 2 to 24 months.

Results—Cases had significantly lower mean standardized scores than controls on measures of cognitive ability and motor functioning ($p < 0.02$). These differences were unaffected by the location of synostosis, age of diagnosis, infant sex, and maternal IQ. Measures of early language functions revealed no group differences.

Conclusions—Before cranioplasty, single-suture craniosynostosis is associated with modest but reliable neurodevelopmental delays that cannot be attributed to maternal intelligence and family sociodemographic variables. Follow-up of this sample will determine the predictive significance of these delays. In the meantime, routine neurodevelopmental screening of infants with isolated craniosynostosis is recommended.

Single-suture craniosynostosis has been associated in several studies with cognitive and motor delays during infancy (both before and after cranioplasty) and heightened risk of learning and language disabilities in school-aged children (for a recent review, see Speltz et al.[1]). Although the causal implications of this association are unclear, this finding has prompted researchers to recommend that infants with singlesuture craniosynostosis be screened routinely for neurodevelopmental problems, and that indications for cranioplasty remain centered on *both* the correction of deformity *and* minimization of neuropsychological problems.[2] However, as several investigators have also noted, the methodologies of most

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studies have suffered from substantial limitations, leaving uncertain the reliability and strength of association between synostosis and neurodevelopment.[3,4] Methodologic limitations have included the absence of control groups; unspecified criteria for the inclusion or exclusion of cases (particularly with respect to the co-occurrence of associated intracranial or extracranial anomalies)[5]; and small sample sizes that have limited statistical power and precluded analyses of functioning by specific sutural diagnosis (e.g., sagittal versus metopic).

The most significant problem at this early stage of research is the lack of control groups. Nearly all studies have compared cases with test norms or estimated base rates of selected problems (e.g., prevalence estimates of learning or language disabilities). This method is flawed, as cases drawn from clinical programs may differ substantially from the samples used to develop test norms or prevalence estimates (e.g., clinical samples may overrepresent or underrepresent urban or rural families, or families with particular socioeconomic backgrounds). Test norms may also become invalid over time, because of changes in population characteristics and/or environmental factors that affect the assessment of development.[6–8] For example, several investigators have documented motor delays in otherwise typically developing infants who were positioned frequently in supine position for sleep as recommended by the American Academy of Pediatrics Back to Sleep campaign.[9,10] The Back to Sleep program is believed to have exerted a widespread influence in the U.S. population.[11] Test norms for instruments developed before Back to Sleep may therefore lead to erroneous conclusions about the developmental status of an index group in relation to these norms. The first and second editions of the Bayley Scales of Infant Development were developed before Back to Sleep and have been used in most U.S. studies of infants with single-suture craniosynostosis.[12–15]

Three previous studies of single-suture craniosynostosis have avoided the test norm problem by using control groups, but all have had very small samples. Virtanen et al. found 18 school-aged children with sagittal synostosis to score significantly lower than controls on several IQ subtests.[16] Boltshauser and colleagues conducted detailed psychological and neuropsychological assessments of 30 unoperated cases of sagittal synostosis (aged 2 to 25 years) and included 17 siblings as controls.[17] Few differences between cases and siblings were found. In the only infancy study to use a control group, Speltz et al. found no differences between 19 infants with and 19 without sagittal synostosis, either before surgery (at about 3 months of age) or afterward (at ages 12 and 24 months).[15]

In an effort to correct or minimize the methodologic limitations of previous studies, we have undertaken a prospective, longitudinal study of 250 infants with and 250 without single-suture fusions. Cases have been recruited from four urban craniofacial centers in the United States. All infants are being assessed at three time points: at the time of initial diagnosis (typically at approximately age 6 months) and at 18 and 36 months of age. In the present article, we report analyses of data collected up to the midpoint of data collection, focusing on comparisons of development before surgery among 125 case-control pairs. Two questions were of central interest. First, in comparison with healthy controls and before cranial release, do infants with single-suture craniosynostosis show delays in mental, psychomotor, and/or early language development? Second, do case-control group differences vary by diagnosis (e.g., sagittal, metopic, or coronal synostosis)? Lekovic et al. hypothesized that children with metopic synostosis are the most severely affected among those with isolated synostoses because metopic fusions are more likely associated with intracranial abnormalities such as agenesis of the corpus collosum.[2] The American Society of Maxillofacial Surgeons Outcome Study recently found in a small sample of infants with single-suture craniosynostosis ($n = 22$) that cases of coronal synostosis had lower Bayley

Scales of Infant Development scores than sagittal cases; however, a control group was not included in this study.[18]

PATIENTS AND METHODS

Participants

Participants included 125 infants with single-suture craniosynostosis and 125 case-matched, healthy infants (controls) and their parents. Participants were enrolled after obtaining informed consent approved by the institutional review boards of the participating centers. This research is in full compliance with Health Insurance Portability and Accountability Act standards. Each participating center (Children's Hospital and Regional Medical Center in Seattle; the Cleft Lip and Palate Institute and Northwestern University in Chicago, Children's Heath Care of Atlanta, and St. Louis Children's Hospital) obtained independent institutional approval.

Cases—Infants were eligible if they (1) had singlesuture craniosynostosis (sagittal, metopic, unilateral coronal synostosis, or unilateral lambdoid synostosis), confirmed by computed tomographic scans; (2) had not yet had reconstructive surgery; and (3) were 30 months of age or younger at the time of recruitment. Exclusion criteria for cases included (1) premature birth (before 34 weeks' gestation); (2) presence of major medical or neurologic conditions (e.g., cardiac defects, seizure disorders, cerebral palsy, significant health conditions requiring surgical correction); (3) presence of three or more extracranial minor malformations as defined by Leppig et al.[19]; or (4) presence of major malformations. Twins were eligible to participate in the study when either one had single-suture craniosynostosis. The 125 enrolled cases represented 89 percent of all eligible cases. Nine families declined to participate, primarily because of distance or time constraints. Six infants were unable to be scheduled before cranial surgery.

Controls—Infants were eligible as controls if they had no known craniofacial anomaly and did not meet any of the exclusionary criteria for cases (described above). Infants with isolated minor medical conditions such as colic, acid reflux disease, or allergies were eligible. Control group participants were recruited through pediatric practices, birthing centers, and announcements in newsletters and/or other publications of interest to parents of newborns. Controls were matched to each case individually in relation to (1) age (*chronologically* within 3 weeks older or younger), (2) sex, (3) family socioeconomic status (within the same Hollingshead four-factor classification),[20] and (4) ethnicity. When there was more than one potentially matching control identified for a particular case, the control participant was selected randomly for approach and/or further screening by telephone. Telephone screening confirmed participants' case-matching status and absence of exclusionary criteria. The 125 enrolled control group participants represented 37 percent of all those who were screened by telephone.

Measures

Bayley Scales of Infant Development, Second Edition—The Bayley Scales of Infant Development, Second Edition, was used to measure infants' cognitive and psychomotor status.[21] It is a standardized, norm-referenced objective test of the infant's developmental status from 16 days to 42 months 15 days of age. The second edition provides updated norms based on 1700 children stratified according to the 1988 updated U.S. census report. It yields separate indices of mental and psychomotor development: the Mental Development Index and Psychomotor Development Index. The manual, *Bayley Scales of Infant Development*, Second Edition, provides information about reliability and

validity. It continues to be one of the best and most frequently used instruments with which to assess infant development.[22]

Language Functioning—The Preschool Language Scale, Third Edition was used to assess expressive and receptive language skills.[23] The Preschool Language Scale, Third Edition is a norm-referenced, individually administered objective test of infant language. Norms are provided for infants and preschoolers from 2 weeks to 83 months of age and are based on the assessment of more than 1900 children stratified according to the 1984 updated U.S. Census report. It yields two scale scores: receptive (Preschool Language Scale, Third Edition Auditory Comprehension) and expressive (Preschool Language Scale, Third Edition Expressive Communication) language and a total language score. Concurrent validity is indicated by positive association between the Denver II and the Preschool Language Scale, Third Edition. Internal consistency scores for the age groups included in this study have ranged from 0.47 to 0.92. Internal consistency is above 0.74 for both scales at all age groups except for the Preschool Language Scale, Third Edition Auditory Comprehension at the age ranges 0 to 2, 6 to 8, and 9 to 11 months, where the scores are 0.47, 0.53, and 0.67, respectively.

Maternal Intelligence—As a potential correlate of child developmental outcomes, maternal intelligence was assessed using the Wonderlic Personnel Test.[24] The Wonderlic Personnel Test is a brief (12-minute), timed paper/pencil test of intelligence standardized on 118,549 teenagers and adults. Validity studies have demonstrated that correlations between Wonderlic Personnel Test scores and Full Scale IQ scores on the Wechsler Adult Intelligence Scale-Revised have ranged from 0.75 to 0.96. Test-retest reliability scores ranged from 0.82 to 0.94 and internal consistency ranged from 0.88 to 0.94. The normative Wonderlic Personnel Test mean is 21.06, with an SD of 7.12.

Examiner Training and Reliability—All Bayley Scales of Infant Development, Second Edition and Preschool Language Scale, Third Edition assessments were performed by trained psychometrists and videotaped for reliability purposes. Before being allowed to test infants in this project, examiners from all sites provided two sample tapes for review and feedback by the second author (K.K.-S.). Approximately 10 percent of all subsequent assessments were independently reviewed to ensure reliability and rescored if necessary. Agreement on individual items was 96.5 percent for the Mental Development Index, 93 percent for the Psychomotor Development Index, and 98.9 percent for both the Preschool Language Scale, Third Edition receptive and expressive language scales.

Procedures

Infants were referred to the project at the time of diagnosis by the treating surgeon or pediatrician. Informed consent was obtained after following the institutional review board–approved protocols of each participating institution. Psychometrists first administered the Bayley Scales of Infant Development, Second Edition and the Preschool Language Scale, Third Edition. Mothers were then individually interviewed to obtain medical history data. They completed the Wonderlic Personnel Test independently in a quiet room.

RESULTS

Table 1 lists selected characteristics of the sample. Of the 125 case-control pairs, 39 percent were female, and the mean age was 6.5 and 6.6 months in cases and controls, respectively. Children with and without craniosynostosis had similar distributions of race and family socioeconomic status. Among craniosynostosis cases, the majority had sagittal synostosis (n = 62), followed by diagnoses of metopic (n = 27), right or left coronal (n = 28), and

lambdoid ($n = 8$). Sex of infant differed by diagnosis, with a larger proportion of male patients in the sagittal and metopic groups (79 and 67 percent, respectively); the left unilateral coronal group was composed only of female patients. These sex differences are consistent with population trends.[4] In addition, sagittal cases tended to be younger than other diagnostic groups. In both groups, approximately 90 percent of children lived in households with both biological parents (not shown). Site of data collection (Seattle, Chicago, St. Louis, and Atlanta) was not associated with any dependent variable or covariate ($p > 0.10$).

Correlations among Measures

Tables 2 and 3 show correlations among measures of developmental status (Bayley Scales of Infant Development, Second Edition and Preschool Language Scale, Third Edition), maternal IQ, family socioeconomic status, and infant age for cases and controls. In both groups, measures of cognitive, language, and motor functions were positively correlated with one another, with correlations ranging from 0.18 to 0.59. Although maternal IQ was positively correlated with socioeconomic status in both groups (0.40 and 0.44 for cases and controls, respectively), maternal IQ was not associated with any measure of infant developmental status. Only one of the four developmental measures was associated with age among cases: the Preschool Language Scale, Third Edition Auditory Comprehension scale (<0.24). Among controls, both the Mental Development Index and the Psychomotor Development Index were directly associated with age (0.21 and 0.20, respectively).

Comparison of Cases and Controls

Table 4 lists group means and standard deviations (in parentheses) for cases and controls on the four developmental measures (Bayley Scales of Infant Development, Second Edition Mental Development Index, Bayley Scales of Infant Development, Second Edition Psychomotor Development Index, Preschool Language Scale, Third Edition Auditory Comprehension and Expressive Communication). Table 4 also lists 95 percent confidence intervals (i.e., estimated range of values in the population) and effect sizes, which indicate the strength of association between group status (case versus control) and each dependent measure. Effect sizes were calculated by dividing group mean differences by pooled standard deviations. Hotelling's t^2 test was used to analyze the mean differences between groups. This procedure minimizes inflation of type I error caused by multiple significance tests with correlated dependent variables, essentially extending the standard t test to analyses of multiple variables. Alpha (criterion for statistical significance) was 0.05.

The overall effect of group was significant ($F = 3.29$; $p = 0.016$). Paired t tests were used to examine group differences on each measure. As shown in Table 4, cases had lower mean Mental Development Index scores (91.9) than controls (94.9; $p = 0.005$). Cases also had lower Psychomotor Development Index scores than controls (mean, 84.1 versus 88.8, respectively; $p = 0.001$). On average, cases scored 2.5 points lower on the Preschool Language Scale, Third Edition Auditory Comprehension scale than did controls, but this difference did not reach statistical significance ($p = 0.069$). No differences between cases and controls were found on the Preschool Language Scale, Third Edition Expressive Communication scale.

Maternal IQ

No statistically significant difference between groups was found for maternal IQ ($p = 0.11$). Both groups scored well within the average range for this instrument. Cases had a mean of 107.05 (SD = 12.08) and controls had a mean of 109.15 (SD = 12.29).

Infant Sex

Table 5 lists means and standard deviations for the four developmental measures by sex. A generalized estimating equation model with robust standard errors was used to test for the possibility that case-control differences on developmental measures differed by sex (i.e., testing the interaction between case status and sex). There was no evidence for interaction on any measure.

Diagnostic Subgroup Differences

As shown in Table 6, mean Mental Development Index scores ranged from 88.3 in right unilateral coronal cases to 95.4 in lambdoid cases. Psychomotor Development Index scores were lowest in children with lambdoid synostosis (78.0) and highest in those with metopic synostosis (86.6). Performance on the Preschool Language Scale, Third Edition Auditory Comprehension and Expressive Communication domains was lowest in the right unilateral coronal group (89.1 and 90.0, respectively). Sagittal cases had the highest scores on the Preschool Language Scale, Third Edition Auditory Comprehension (93.7), whereas left unicoronal cases had the highest scores on the Preschool Language Scale, Third Edition Expressive Communication (102.7). Case-control differences in test performance across diagnostic subgroups were tested with linear regression models including a “dummy” variable for craniosynostosis diagnosis. Separate regressions were conducted for each of the four test scores. The sagittal group served as the reference group, as it contained the largest number of participants. These analyses found no significant group differences in case-control comparisons for any measure ($p = 0.05$).

DISCUSSION

Infants with single-suture craniosynostosis had lower scores on both scales of the Bayley Scales of Infant Development, Second Edition than healthy infants matched for age, infant sex, family socioeconomic status, and ethnicity. This finding was unaffected by maternal IQ and infant age and sex. Measures of language functions revealed no group differences in expressive or receptive abilities during the age range encompassed by this first evaluation of our cohort.

From a clinical standpoint, the magnitude of group differences on the Bayley Scales of Infant Development, Second Edition was relatively small, with the mean scores of all groups within—or very close to—the “normal” range of functioning. The comparability of scores between cases and controls highlights the importance of including a control group in this type of research. In the absence of control group data, the effect of single-suture craniosynostosis on Bayley Scales of Infant Development, Second Edition motor scores would have appeared much greater in relation to test norms (i.e., 16 points or just over 1 SD) than the casecontrol group differences actually obtained (i.e., just under 5 points, or 0.3 SD). It is possible that the relatively low motor scores for both groups are related to the Back to Sleep recommendations, as previous research has documented transitory delays in motor development at 6 months for otherwise typically developing infants.[10]

The design of the study does not allow us to unequivocally determine the sources or causes of group differences. They may be directly related to the presence (or absence) of craniosynostosis or related to other factors associated with this condition (e.g., underlying neuropathologic abnormalities affecting both skull and brain; environmental stress on infant and/or parent).[1]

Although the diagnostic subgroups varied among themselves, there was no evidence that participants in any of the diagnostic subgroups were more or less likely to differ from controls. It is likely that an adequate test of such differences will require assessment of this

cohort at an older age point (e.g., school-age), when children can be evaluated with measures more sensitive to specific brain– behavior relations, such as those targeting interhemispheric tasks or executive functions. Furthermore, the small number of infants in most of our subgroups (e.g., unilateral coronal and lambdoid) limited the power of statistical testing. As we collect the remainder of our sample (which will double in size), we will have a better statistical opportunity to assess these differences.

Among both cases and controls, we found that test scores showed some degree of correlation with age of testing. Associations between test performance and test age in infants with single-suture craniosynostosis before cranioplasty have been of interest to investigators because they provide an indirect test of the hypothesis that intracranial pressure is inversely related to the neurodevelopment of these infants.[25–27] It has been hypothesized that later diagnosis and surgery is associated with prolonged exposure to higher levels of intracranial pressure and, consequently, compromised brain development, leading to inverse relations between test scores and test age among cases. No association between age and performance would be expected among controls.[27] The pattern of correlations in this study provides little support for this hypothesis, despite a reasonably broad range of ages among participants (2 to 24 months). Among cases, there was near zero correlation between age and three of the four developmental measures given; the one exception (Preschool Language Scale, Third Edition Auditory Comprehension) yielded a modest, inverse correlation (<0.24).

CONCLUSIONS

The clinical implications of the case-control group differences in this study will remain uncertain until we conduct planned longitudinal follow-ups to examine the predictive significance of these data in relation to later developmental outcomes (e.g., Bayley Scales of Infant Development, Second Edition scores at age 3, which have been associated with school age achievement).[22] Nevertheless, until such data are available, we would support the recommendation of previous investigators that infants with single-suture craniosynostosis be screened routinely for neurodevelopmental problems through craniofacial programs.[1,2] Neurodevelopmental outcomes are likely to be quite heterogeneous in this population (even within the same diagnosis), and infants at particularly high risk (e.g., Bayley Scales of Infant Development, Second Edition scores <80) could be targeted for preventative interventions with proven efficacy.[28] Continued study of this sample will help determine the specific clinical and demographic predictors of neurobehavioral outcomes, which should enhance future efforts to identify and treat high-risk cases.

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Table 1

Selected Characteristics of Cases and Controls at Presurgery Visit

Characteristic	Sagittal (*n* = 62)	Metopic (*n* = 27)	Right Unicoronal (*n* = 16)	Left Unicoronal (*n* = 12)	Lambdoid (*n* = 8)	Total Cases (*n* = 125)	Total Controls (*n* = 125)
Child sex							
Female	13 *	9	10	12	5	49 (39) †‡	49 (39)
Male	49	18	6	0	3	76 (61)	76 (61)
Child age							
<3.5 months	23	1	0	0	0	24 (19)	21 (17)
3.5–6.5 months	23	10	10	5	2	50 (40)	52 (42)
6.51–9.5 months	9	8	3	4	3	27 (22)	29 (23)
9.51–12.5 months	6	4	1	2	3	16 (13)	16 (13)
12.5+ months	1	4	2	1	0	8 (6)	7 (6)
Mean (SD)						6.5 (3.9)	6.6 (3.9)
Child ethnicity							
Caucasian	48	19	13	8	6	94 (75)	98 (78)
Other	14	8	3	4	2	31 (25)	27 (22)
SES score							
I (high)	15	4	3	4	3	29 (23)	28 (22)
II	35	15	6	5	3	64 (51)	67 (54)
III	7	5	7	1	2	22 (18)	19 (15)
IV	3	1	0	0	0	4 (3)	5 (4)
V (low)	2	2	0	2	0	6 (5)	6 (5)
Site							
Seattle	24	11	5	6	3	49 (39)	49 (39)
Chicago	9	13	6	4	4	36 (29)	36 (29)
St. Louis	13	0	4	1	1	19 (15)	19 (15)
Atlanta	16	3	1	1	0	21 (17)	21 (17)

SES, socioeconomic status.

*No. of individuals.

†No. of individuals (%).

[‡] Percentages may not add up to 100 because of rounding error.

Table 2

Correlations for Cases among Infant Test Scores, Mother's IQ, Family Socioeconomic Status, and Infant Age*

	BSID-II MDI	BSID-II PDI	PLS-AC	PLS-EC	WAIS IQ	SES	Age
BSID-II MDI	1.00						
BSID-II PDI	0.59†	1.00					
PLS-AC	0.25†	0.18*	1.00				
PLS-EC	0.36†	0.26†	0.33†	1.00			
WAIS IQ	0.14	0.14	−0.07	0.03	1.00		
SES	−0.01	0.02	0.10	−0.04	0.40†	1.00	
Age	0.04	0.06	−0.24†	−0.03	−0.06	−0.03	1.00

BSID-II, Bayley Scales of Infant Development, Second Edition; MDI, Mental Development Index; PDI, Psychomotor Development Index; PLS, Preschool Language Scale, Third Edition; AC, Auditory Comprehension; EC, Expressive Communication; WAIS, Wechsler Adult Intelligence Scale; SES, socioeconomic status.

*$p < 0.05$.

†$p < 0.025$.

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Table 3

Correlations for Controls among Infant Test Scores, Mother's IQ, Family Socioeconomic Status, and Infant Age*

	BSID-II MDI	BSID-II PDI	PLS-AC	PLS-EC	WAIS IQ	SES	Age
BSID-II MDI	1.00						
BSID-II PDI	0.53†	1.00					
PLS-AC	0.30†	0.18*	1.00				
PLS-EC	0.39†	0.18*	0.40†	1.00			
WAIS IQ	−0.08	−0.18	0.10	0.14	1.00		
SES	0.11	−0.13	0.07	0.10	0.44†	1.00	
Age	0.21†	0.20*	−0.16	0.01	−0.06	−0.06	1.00

BSID-II, Bayley Scales of Infant Development, Second Edition; MDI, Mental Development Index; PDI, Psychomotor Development Index; PLS, Preschool Language Scale, Third Edition; AC, Auditory Comprehension; EC, Expressive Communication; WAIS, Wechsler Adult Intelligence Scale; SES, socioeconomic status.

*$p < 0.05$.

†$p < 0.025$)

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Table 4

Univariate Comparisons of Mean Neurobehavioral Test Scores for Cases versus Matched Controls (Paired *t* Tests)

Test Measure	No. of Pairs	Cases, Mean (SD)	Controls, Mean (SD)	Difference		Effect Sizes†	*p*
				Mean (SD)	95% CI		
BSID-II MDI	125	91.92 (9.19)	94.89 (8.52)	−2.97 (11.56)	−5.02 to −0.92	−0.34	0.005
BSID-II PDI	125	84.0 (12.03)	88.82 (11.31)	−4.74 (15.91)	−7.56 to −1.93	−0.41	0.001
PLS-3 AC*	123	91.97 (13.13)	94.46 (11.74)	−2.50 (15.07)	−5.19 to 0.19	−0.20	0.069
PLS-3 EC*	124	96.65 (14.45)	97.31 (13.48)	−0.6 (18.34)	−3.92 to 2.60	−0.05	0.689
Maternal IQ	105	107.05 (12.08)	109.15 (12.29)	−2.10 (13.24)	−4.67 to 0.46	−0.17	0.106

CI, confidence interval; BSID-II, Bayley Scales of Infant Development, Second Edition; MDI, Mental Development Index; PDI, Psychomotor Development Index; PLS, Preschool Language Scale, Third Edition; AC, Auditory Comprehension; EC, Expressive Communication.

*Standard score.

†Mean difference effect size.

Table 5

Comparisons of Mean (SD) Test Scores by Sex

	Female Patients			Male Patients			
Variable	**Cases (*n* = 49)**	**Controls (*n* = 49)**	**Difference (Case – Control)**	**Cases (*n* = 76)**	**Controls (*n* = 76)**	**Difference (Case – Control)**	***p****
BSID-II MDI	92.53 (10.63)†	95.61 (7.62)	−3.08 (13.38)	91.53 (8.17)	94.42 (9.07)	−2.89 (10.32)	0.933
BSID-II PDI	84.71 (12.46)	90.02 (10.43)	−5.31 (16.15)	83.67 (11.81)	88.05 (11.84)	−4.38 (15.86)	0.752
PLS-AC‡	91.06 (11.42)	96.00 (12.18)	−4.56 (16.47)	92.55 (14.16)	93.67 (11.51)	−1.17 (14.06)	0.196
PLS-EC§	95.96 (14.34)	95.12 (11.16)	0.84 (19.09)	97.11 (14.61)	98.63 (14.63)	−1.64 (17.89)	0.484

BSID-II, Bayley Scales of Infant Development, Second Edition; MDI, Mental Development Index; PDI, Psychomotor Development Index; PLS, Preschool Language Scale, Third Edition; AC, Auditory Comprehension; EC, Expressive Communication.

*Test of interaction between sex and group status (case vs. control) from generalized estimating equation model.

†Standard deviations are in parentheses.

‡PLS-AC data are missing for one female patient and one male patient.

§PLS-EC data missing for one male patient.

Table 6

Comparisons of Mean Test Scores across Diagnostic Groups*

Variable	Sagittal (*n* = 62)	Metopic (*n* = 27)	Right Unicoronal (*n* = 16)	Left Unicoronal (*n* = 12)	Lambdoid (*n* = 8)
BSID-II MDI	90.85 (9.05)	94.52 (7.32)	88.25 (13.57)	94.17 (5.98)	95.38 (6.46)
BSID-II PDI	84.27 (10.58)	86.63 (13.56)	81.06 (13.32)	85.42 (6.13)	78.00 (19.32)
PLS-AC†	93.65 (14.20)	90.37 (12.36)	89.06 (10.63)	92.67 (13.00)	89.50 (12.99)
PLS-EC‡	97.39 (15.33)	97.78 (14.57)	90.00 (11.35)	102.67 (12.11)	91.50 (12.63)

BSID-II, Bayley Scales of Infant Development, Second Edition; MDI, Mental Development Index; PDI, Psychomotor Development Index; PLS, Preschool Language Scale, Third Edition; AC, Auditory Comprehension; EC, Expressive Communication.

*All comparisons of case-control differences across diagnostic groups (using sagittal as the reference group) were nonsignificant ($p > 0.05$). Standard deviations are in parentheses.

†PLS-AC data missing for two sagittal cases.

‡PLS-EC data missing for one sagittal case.

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