Neurodevelopment in Children with Single-Suture Craniosynostosis and Plagiocephaly without Synostosis

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The objective of this study was to determine whether children with nonsyndromic craniosynostosis and plagiocephaly without synostosis demonstrated cognitive and psychomotor delays when compared with a standardized population sample. This was the initial assessment of a larger prospective study, which involved 21 subjects with nonsyndromic craniosynostosis (mean age, 10.9 months) and 42 subjects with plagiocephaly without synostosis (mean age, 8.4 months). Each child was assessed using the Bayley Scales of Infant Development–II (BSID-II) for cognitive and psychomotor development before therapeutic intervention (surgery for craniosynostosis and molding-helmet therapy for plagiocephaly without synostosis). The distribution of the scores was divided into four groups: accelerated, normal, mild delay, and significant delay. The distributions of the mental developmental index (MDI) and the psychomotor developmental index (PDI) were then compared with a standardized Bayley’s age-matched population, using Fisher’s exact chi-square test. Within the craniosynostosis group, the PDI scores were significantly different from the standardized distribution \( p < 0.001 \). With regard to the PDI scores, 0 percent of the subjects in the craniosynostosis group were accelerated, 43 percent were normal, 48 percent had mild delay, and 9 percent had significant delay. In contrast, the MDI scores were not statistically different \( (p = 0.08) \). Within the group with plagiocephaly without synostosis, both the PDI and MDI scores were significantly different from the normal curve distribution \( (p < 0.001) \). With regard to the PDI scores, 0 percent of the subjects in the group with plagiocephaly without synostosis were accelerated, 67 percent were normal, 20 percent had mild delay, and 13 percent had significant delay. With regard to the MDI scores, 0 percent of the subjects in this group were accelerated, 83 percent were normal, 8 percent had mild delay and 9 percent had significant delay. This study indicates that before any intervention, subjects with single-suture syndromic craniosynostosis and plagiocephaly without synostosis demonstrate delays in cognitive and psychomotor development. Continued postintervention assessments are needed to determine whether these developmental delays can be ameliorated with treatment. (Plast. Reconstr. Surg. 108: 1492, 2001.)

As the debate regarding the etiology of craniosynostosis continues, the role of the dura and the underlying brain is taking credence over theories that incriminated the cranial base and the cranial sutures. The precise effect of the fused suture on the underlying cortex is unknown. Does the fused suture restrict the growth of the cortex, thereby blunting the gyri and the sulci? Or is the blunted cortex the primary cause in signaling the dura to fuse prematurely? Irrespective of the primary event, the underlying cortex does demonstrate blunting, as has been demonstrated by magnetic resonance imaging scans of subjects with craniosynostosis.1 Numerous investigators have attempted to elucidate the effect of the cortical abnormalities on mental development.2–4 Most studies have been retrospective and have not involved a longitudinal follow-up.5 Others have not used a standardized format or assessment tools.6 This study was initiated as a prospective assessment of mental and psychomotor development in children with single-suture craniosynostosis without a clinically identifiable syndrome. Assessments were performed both before and 1 year after surgery. This study reports the results of the initial preoperative assessment.

Deformational plagiocephaly or plagiocephaly without synostosis became more prevalent in 1992 when the American Association of Pediatricians recommended that parents should place their children in the supine position to reduce the incidence of sudden infant death syn-
The soft calvarium deformed under the gradual pressure, leading to occipital nonsynostotic plagiocephaly. The effect of the flattened occipital calvarium on the underlying cortex has not been studied and is therefore unknown. Some researchers also believe that the calvarium deforms during the final months of intrauterine life when it is compressed against the mother’s pelvic brim or the lumbosacral spine. With the study presented, we sought to detect developmental delays, if any, in children with plagiocephaly without synostosis.

**Patients and Methods**

**Study Population**

Twenty-one consecutive children with radiographically confirmed, isolated, nonsyndromic, craniosynostosis who had not undergone surgery (11 sagittal, five metopic, two biconoral, and three unicoronal cases of synostosis) and 42 consecutive children with radiographically confirmed plagiocephaly without synostosis were enrolled in this prospective protocol between 1997 and 1999. The mean ages of the craniosynostosis subjects and the subjects with plagiocephaly without synostosis were 10.9 and 8.4 months, respectively.

**Neurodevelopmental Assessment**

All children were assessed by the same licensed psychologist and licensed professional counselor in the Department of Pediatrics at the University of Oklahoma Health Sciences Center. The infants were assessed using the Bayley Scales of Infant Development–II (BSID-II). The BSID-II is a standardized measure that provides indices of development: the mental developmental index (MDI) and psychomotor developmental index (PDI). It is designed for use with infants 1 month to 42 months of age. The BSID-II was standardized on 1700 subjects with 100 children in each of the 17 age groups delineated in the scales. The MDI assesses cognitive, language, and personal/social abilities. The PDI addresses fine and gross motor skills. The measure has a mean of 100 with an SD of 15. The score is derived by comparing the child’s performance with a standardized same-age sample. The BSID-II is considered to be a highly reliable assessment tool (MDI $r = 0.88$; PDI $r = 0.84$). Stability of the test for the entire age samples ranged from $r = 0.87$ on the mental portion of the test to $r = 0.78$ on the motor portion. Four constructs have been identified in the BSID-II: cognitive, language, motor, and personal/social. For the subjects in this study’s sample, there was a focus on early language skills (e.g., vowel-consonant combinations, jabbering, and early word production), problem-solving abilities, imitation skills, fine motor abilities such as grasping objects, and gross motor skills (e.g., balance, early walking or crawling abilities, and coordination).

Administration of the BSID-II is a specialized skill requiring expertise in the areas of infant/child development. Any administrators of this instrument should have training in the administration and interpretation of comprehensive and developmental skill measurements. Generally, examiners who use the BSID-II have formal graduate training in child assessment. The BSID-II takes approximately 1 to 1½ hours to administer to each child being assessed. In our study, the infants’ caregivers were present during the assessments.

Although studies of the BSID-II and later child development have been conducted, the purpose of the measure is to sample emerging developmental abilities and milestones. Studies predicting later development primarily address preschool-age children. For example, children considered to be at-risk and showing developmental delays at 12 months correlated with scores of development at 4.5 years of age. Similarly, at-risk children assessed at 6 months had scores predictive of intelligence scores at 24 and 48 months.

The BSID-II was administered before cranial-vault remodeling or molding-helmet therapy treatment methods were used. Each child was assessed for mental and motor development, resulting in an MDI and a PDI. Each score was classified as within normal limits if the score was between 85 and 115 (+1 SD to −1 SD); mildly delayed for a score between 70 and 84 (between −1 SD and −2 SD); and severely delayed for scores less than 67 (> −2 SD). Similarly, scores above 117 (> 1 SD) were classified as accelerated. The cognitive portion of the study was administered with the child seated at a table while on the caregiver’s lap and/or lying on the floor. The motor portion was conducted with the child on the floor. If the child was walking, several items were completed in a physical therapy motor room.

**Methods**

Each child’s score was documented for mental and motor development. On the basis of the score, the children were placed in the above-
mentioned groups. The frequency distribution of the scores was compared with the expected frequency derived from the BSID-II standardized sample.

The age at diagnosis was compared with the severity of scores to see whether there was any correlation between them. Similarly, the type of medical insurance was compared with the severity of the scores in an attempt to correlate the scores and socioeconomic status.

Statistical Methods

Because there were some outliers within the sample, medians were used instead of means. The distribution of developmental scores into four categories was compared with the expected distribution of scores, on the basis of the standardized BSID-II, using an exact chi-square goodness-of-fit test. This procedure accounts for the small sample size. When the pairwise correlations were examined, Spearman’s rho was used. When the difference in the MDI or PDI was compared by Medicaid status, the Wilcoxon rank sum test was used.

RESULTS

Group 1: Craniosynostosis

When MDI scores were compared, the distribution of craniosynostosis scores was not found to be significantly different from the standardized distribution \((p = 0.166)\). The striking difference in the distributions was the lack of any craniosynostosis children in the accelerated category. The percentage of children in the within normal limits category was higher than the percentage expected (76.2 percent versus 68 percent). However, the percentage of children categorized with mild or severe delays was also increased (Table I).

When the PDI scores were compared, the craniosynostosis scores were significantly different from the distribution expected \((p < 0.001)\). Again, no children in the craniosynostosis group had scores in the accelerated range of functioning. The percentage of children in the within normal limits category was lower than that expected for the general population. The percentage of children in the within normal limits range was 42.9 percent, compared with the expected 78 percent. The percentage of children within the mildly delayed and severely delayed ranges of functioning were 47.6 percent and 9.5 percent, respectively, compared with 13.5 and 2.5 found in a standardized theoretical normal distribution (Table II).

Group 2: Plagiocephaly without Synostosis

When the MDI scores were compared, the scores for plagiocephaly without synostosis were found to be significantly different from the standardized distribution expected \((p = 0.002)\). Although no children were identified in the accelerated range of functioning, more children than expected were identified as functioning within normal limits (82.6 percent versus 68.0 percent). The percentage of children within the group with plagiocephaly without synostosis who were categorized as severely delayed was significantly higher than that expected (8.7 percent versus 2.5 percent) (Table I). Analysis of these subjects’ PDI scores indicated significant differences between PDI performance in the studied population, compared with the standardized population \((p < 0.001)\). As with the MDI, none of any children in the plagiocephaly without synostosis sample scored within the accelerated range of functioning. Perhaps one of the most striking findings was the significant percentage of children falling in the mildly delayed or severely delayed range of functioning, compared with the standardized distribution (Table II).

### Table I

<table>
<thead>
<tr>
<th>MDI Score Groups</th>
<th>Standardized Distribution (%)</th>
<th>Craniosynostosis</th>
<th>Deformational Plagiocephaly</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Accelerated</td>
<td>16.5</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Normal</td>
<td>68.7</td>
<td>16</td>
<td>76.2</td>
</tr>
<tr>
<td>Mild delay</td>
<td>12.5</td>
<td>4</td>
<td>19.1</td>
</tr>
<tr>
<td>Severely delayed</td>
<td>2.3</td>
<td>1</td>
<td>4.8</td>
</tr>
<tr>
<td>Total number</td>
<td></td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

\(p^*\) is for the chi-square goodness-of-fit test comparing each study group with the standard.

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Age Analyses

The age of the child was not significantly correlated with either the MDI or the PDI. For the craniosynostosis group, the age-MDI correlation coefficient was 0.10, and that for age-PDI group, 0.11. For the group with plagiocephaly without synostosis, the age-MDI correlation coefficient was −0.10, and that for the age-PDI group, −0.19.

Health-Coverage Analyses

MDI. Within the craniosynostosis group, nine children with Medicaid coverage were compared with 11 children with other health-care coverage. The MDI scores for the craniosynostosis group did not differ significantly for those subjects with health-care coverage (p = 0.201); the mean MDI for the craniosynostosis sample covered by Medicaid was 82.9 (SD, 13.6) and that for the craniosynostosis sample of subjects covered by other health-care plans was 90.7 (SD, 8.1). For the group with plagiocephaly without synostosis, the MDI scores for the 14 children with Medicaid coverage were also not significantly different from those of the 32 children with other health-care coverage [p = 0.138; means, 84.4 (SD, 16.9) and 91.7 (SD, 12), respectively].

PDI. For the craniosynostosis group, the PDI outcome showed no significant difference between the children with Medicaid coverage and those with other coverage [p > 0.5; means, 82.0 (SD, 13.2) and 85.4 (SD, 16), respectively]. Similarly, for the group with plagiocephaly without synostosis, no significant difference was found between the two types of health-care coverage (p = 0.199), with a mean of 81.6 (SD, 14.1) for those with Medicaid coverage and a mean of 87.9 (SD, 11.7) for those with other health-care coverage.

Although statistical significance was not reached in any of the above comparisons for health-care coverage, the scores for the children in the other insurance group were consistently higher than those in the Medicaid group.

Discussion

Craniosynostosis or the premature fusion of calvarial sutures may involve a single or multiple sutures. Multiple-suture craniosynostosis is commonly associated with abnormalities of other organ systems and manifests with varying degrees of developmental delays. In contrast, single-suture craniosynostosis does not commonly involve multiple organ systems and is not commonly associated with significant developmental delays. However, the association of minor developmental delays and minor learning disabilities with single-suture craniosynostosis is controversial. This association has been the subject of numerous studies and is predominantly related to the recent surge of research involved in elucidating the primary cause of craniosynostosis.2–6

The etiology of craniosynostosis continues to remain unclear. Virchow13 initially proposed that the cranial suture in cases of craniosynostosis was abnormal and therefore responsible for premature closure. Moss and Young14 proposed that the cranial base in craniosynostosis was abnormal and that the dura over the cranial base transmitted abnormal forces to the calvarial sutures, resulting in their premature closure. A recent study by Eaton et al.15 investigated the ritual of three Native American tribes who intentionally bound an infant’s head after birth. Examination of the skulls of these infants led to the conclusion that a primary alteration of the calvarial shape leads to a secondary deformation of the cranial base and not vice versa.
Recent studies have focused on the underlying dura’s being abnormal.16–18 The dura sends abnormal signals to overlying suture, leading to its premature closure. However, the reason for the generation of the abnormal signal by the dura is unknown. Is it a result of an abnormality of the underlying cortex, which is genetically programmed not to grow normally? Does lack of the expansile thrust by the underlying cortex initiate a cascade, resulting in the generation of abnormal signals by the overlying dura and precipitating an early closure of the calvarial suture? The role of the underlying cortex in premature closure has, unfortunately, not been well documented. Topographic analysis of the cortex, using magnetic-resonance imaging scans of children with single-suture craniosynostosis, has revealed that the gyri and sulci are blunted under the abnormal suture.1 Similarly, positron emission tomography scans studying the uptake of radioisotopically tagged glucose have revealed a decreased uptake of glucose in the cortex underlying the prematurely fused suture.19 Whether the abnormality of the cortex is the primary event or is secondary to the effect of the pressure of the overlying abnormally shaped calvarium is, however, unknown. Irrespective of the sequence of the events, the association between the abnormality of the cortex and any minor learning disabilities needs to be studied.

Previous studies have attempted to elucidate the relationship between nonsyndromal craniosynostosis and mental developmental delays. Kapp-Simon et al.2 studied 45 subjects with nonsyndromic craniosynostosis, 25 of whom were reevaluated after undergoing cranial-vault remodeling. The BSID were used for analysis. The mean score of the subjects with craniosynostosis was 103 (SD, 15.8), which was not different from that of the typical population. However, the BSID did not differentiate between mental and motor functioning, as does the BSID-II.

Speltz et al.4 compared the mental and psychomotor development of infants with nonsyndromic sagittal synostosis and compared them with demographically and age-matched subjects without congenital defects. A repeated-measures multivariate analysis of variance test revealed no statistically significant differences between the frequency of mental retardation (> −2 SD) within the two groups. However, the study did not specifically compare the incidence of minor developmental delays between the two groups.

This issue was addressed by Kapp-Simon in a presentation in which she detected a trend toward an increased incidence of learning disorders, which were often characterized by deficits of executive functions in children with nonsyndromic craniosynostosis. In her later study of global intellectual development and learning disorders of children with nonsyndromic craniosynostosis, she did not detect a variation in the normal distribution. However, she did document an increased incidence of mental retardation in children with nonsyndromic craniosynostosis that was two to three times the expected frequency, on the basis of normative data.20

Similarly, two other studies documented an increased incidence of minor learning disorders in children with isolated sagittal synostosis and isolated metopic synostosis.21,22 Kapp-Simon20 also documented an increased frequency of learning disorders in similar subjects. This raises the issue of whether the detection of minor mental and psychomotor delays is more pertinent for these subjects rather than the detection of severe developmental delays (i.e., mental retardation). The extent of cortical impairment may not be severe enough to result in global severe developmental delays resulting in mental retardation but may be focal and result only in minor developmental delays and minor learning disorders.

The study presented here sought to examine the prevalence of developmental delay in two different groups of children with cranial anomalies, compared with a standardized sample of children. Interestingly, the current sample did not find any children in the accelerated range of either mental or motor development that occurs in the normal population. The study also found a significant increase in the number of children with developmental delays, compared with the standardized sample, particularly in the area of motor development. This correlates with published findings of older children who demonstrate minor learning disorders.

The study also sought to examine the incidence of developmental delays in children with plagiocephaly without synostosis. Plagiocephaly without synostosis occurs as a result of prenatal compression of the cranium between the mother’s pelvic brim and lumbosacral spine and
as a result of various abnormal uterine constraints such as oligohydramnios, uterine malformations, fetal malpositions, and multiple fetuses. More commonly, it is secondary to a deformational force that occurs from the child’s lying in the supine position in the early perinatal period. Irrespective of the etiology, the calvarium becomes compressed in the occipital region ipsilaterally and the frontal region contralaterally, resulting in a parallelogram-shaped head. The effect of the abnormally shaped calvarium on the underlying cortex has not been a focus of a study until recently. It has been presumed (by others and by us) that plagiocephaly without synostosis is not associated with any developmental delay.

We sought to question this presumption by performing a developmental analysis of children who had plagiocephaly without synostosis before those children were treated with molding-helmet therapy. Miller and Clarren performed a review of 254 patients with plagiocephaly without synostosis and documented the need of special education and assistance in 39.7 percent of children with the condition, compared with 7.7 percent of siblings within these families. Yet another study by a pediatrician documented that children who slept predominantly in the supine position had poor motor tone and recommended that children should sleep or at least play in the prone position for few hours every day to develop better muscle tone.

Neither the age at diagnosis nor the type of health insurance carrier had a significant effect on the neurodevelopmental scores. Ideally our study would have used a matched sample of children without any cranial anomalies for comparison rather than relying solely on a standardized sample of age-matched children.

We would be remiss in our discussion of this subject if we did not comment on the long-term consequences of the developmental delays. The first question that needs to raised is whether the BSID-II scores are representative of the future outcome: that is, is there a good correlation between the initial test scores and performance at a later age? The scores of children considered to be at-risk, showing delays at 12 months, did correlate with scores of development at 4.5 years of age. Similarly, at-risk children assessed at 6 months had scores predictive of intelligence scores at 24 and 48 months. Understandably, a 3-month-old infant cannot be tested for language delays, but the BSID-II is a comprehensive test and tests various aspects of an infant’s developmental skills, not isolated findings. All these factors make the BSID-II is the most reliable assessment tool for infants. The second question that is raised is whether these findings have long-term consequences. Because the average age of this study population was only 10.9 months, it is impossible to determine whether this subset will develop minor or major learning disorders. These infants need to be studied annually in a prospective fashion. Because two other studies documented that some of these children have long-term minor learning disorders and that children who do and do not undergo surgery for the treatment of these conditions had similar findings, it is possible that the underlying cause for the craniosynostosis is cortical. Continued evaluation of the children in this study’s sample will be necessary to determine the long-term developmental outcome.

It will be equally important to continue to observe these children with plagiocephaly without synostosis after they complete their molding-helmet therapy to assess their long-term developmental progress. The presence of mild developmental delays should not be used as an indication for a surgical intervention. It is possible that the decreased posterior cranial fossa volume caused by the ipsilateral flattening could result in some focal restriction of the underlying occipital cortex. To test this hypothesis, we are currently studying the visual fields of children with plagiocephaly without synostosis.

We continue to observe these infants with nonsyndromic craniosynostosis and plagiocephaly without synostosis not only to obtain longitudinal follow-up data but also to determine the effect of a therapeutic intervention (i.e., cranial-vault modeling for craniosynostosis and molding-helmet therapy for plagiocephaly without synostosis).

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