Case-Control Study of Neurodevelopment in Deformational Plagiocephaly

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Abstract

OBJECTIVE—We assessed the neurodevelopment of infants with and without deformational plagiocephaly (DP), at an average age of 6 months.

METHODS—The Bayley Scales of Infant Development III (BSID-III) were administered to 235 case subjects and 237 demographically similar, control participants. Three-dimensional head photographs were randomized and rated for severity of deformation by 2 craniofacial dysmorphologists who were blinded to case status.

RESULTS—We excluded 2 case subjects with no photographic evidence of DP and 70 control subjects who were judged to have some degree of DP. With control for age, gender, and socioeconomic status, case subjects performed worse than control subjects on all BSID-III scales and subscales. Case subjects' average scores on the motor composite scale were ~10 points lower than control subjects' average scores ($P < .001$). Differences for the cognitive and language composite scales were ~5 points, on average ($P < .001$ for both scales). In subscale analyses, case subjects' gross-motor deficits were greater than their fine-motor deficits. Among case subjects, there was no association between BSID-III performance and the presence of torticollis or infant age at diagnosis.

CONCLUSIONS—DP seems to be associated with early neurodevelopmental disadvantage, which is most evident in motor functions. After follow-up evaluations of this cohort at 18 and 36 months, we will assess the stability of this finding. These data do not necessarily imply that DP

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causes neurodevelopmental delay; they indicate only that DP is a marker of elevated risk for delays. Pediatricians should monitor closely the development of infants with this condition.

Keywords

plagiocephaly; neurodevelopmental; Back to Sleep campaign

Deformational plagiocephaly (DP) refers to cranial asymmetry or symmetric brachycephaly resulting from external forces that shape the infant's skull. Although DP is considered a purely cosmetic problem by many practitioners, several studies have challenged this view. Infants with DP tended to score in the below-average range for cognitive and motor development, compared with normative values from the Bayley Scales of Infant Development II.[1–3] Infants with DP also scored lower than unaffected control subjects in a standardized neurologic examination and a parent-report measure of development.[4] Less is known about later development, although in 2 retrospective studies preschool- and school-aged children with histories of DP were more likely to receive special education or related services than were unaffected siblings[5] or children in the general population.[6]

These findings, although suggesting an association between DP and compromised development, are far from conclusive. Case samples were small, parent reports might have been biased by awareness of the skull deformity, and confounding factors such as socioeconomic status (SES), age, and gender were inadequately controlled. Moreover, the ascertainment of case subjects in previous studies might have led to biased estimates of functioning. For example, infants referred to a DP specialty clinic may be more likely to have other developmental problems than nonreferred infants with similar head shapes, a possibility that can be examined only by including head shape classifications of both referred and nonreferred infants.

We undertook a longitudinal study of 235 infants with diagnosed DP and 237 nonreferred, demographically similar infants without a known history of DP or other craniofacial anomalies. All participants received neurodevelopmental assessments in infancy, at an age corresponding to case subjects' initial diagnosis of DP (~6 months, on average). We assessed the presence and severity of asymmetric and symmetric brachycephalic head shapes among case and control subjects by having expert dysmorphologists rate 3-dimensional images of infants' heads. We evaluated the hypothesis that infants with DP would show poorer cognitive, language, and motor development, compared with unaffected infants, after adjustment for potential confounding factors. Because torticollis is commonly associated with DP and may impair motor development,[7,8] we also examined the association between torticollis and case subjects' neurodevelopmental status.

METHODS

Participants

Consent—Participants were enrolled after informed consent, approved by the institutional review board of Seattle Children's Hospital, was obtained. This research was in full compliance with Health Insurance Portability and Accountability Act standards.

Case Subjects—Infants who were referred for evaluation of DP in the craniofacial center at Seattle Children's Hospital were approached at the time of their diagnosis. Infants were eligible if they received a diagnosis of DP and were between the ages of 4 and 11 months. Exclusions included (1) prematurity (<35 weeks of gestation); (2) a known neurodevelopmental condition (eg, Down syndrome), brain injury, or significant vision or hearing impairment; (3) major malformations or 3 "typical" extracranial anomalies (eg,

extra digits, skin tags, or ptosis); (4) hemifacial microsomia; (5) a non–English-speaking mother; (6) a history of adoption or out-of-home placement; and (7) current family plans to move out of state before completion of this project. Case subjects were seen for their initial study visit within 3 weeks after diagnosis, on average (SD: 1.0). These 235 enrolled case subjects represented 52% of all eligible case subjects. Two hundred three families (45%) declined to participate. Another 15 families (3%) consented to take part in the study but their study visits could not be scheduled within our allotted time interval.

Control Subjects—Infants were eligible for participation in the control sample if they had not been diagnosed as having DP or any other craniofacial anomaly and they did not meet any of the exclusionary criteria for case subjects described above. All except the first 8 control subjects (who were recruited through pediatricians' practices) were identified through an infant participant pool, which consisted of families residing in King and Snohomish counties in Washington State who agreed at the time of their child's birth to be contacted for research participation. Families with a child in the target age range were contacted via telephone. Respondents who expressed interest completed a brief telephone screen for determination of eligibility. The 237 enrolled control group participants represented 90% of all those who were screened via telephone and were determined to be eligible. Twenty-seven families declined participation.

Measures

Severity of Cranial Deformation—Cranial images of all participants' heads were obtained by using a 12-camera, 3dMDCranial, active stereo-photogrammetry system (3dMDCranial System, Atlanta, GA). This system allows for 360° imaging of the head, with a capture speed of <2 milliseconds. A wig cap was placed on each participant, to eliminate hair artifacts. Surface images of the head were deidentified, assigned randomly, and then viewed and rated by 2 dysmorphologists (Drs Heike and Cunningham). Raters were blinded to case-control status. A 4-point severity scale (0 = none, 1 = mild, 2 = moderate, 3 = severe) was used to rate the overall severity of cranial deformation. Both symmetric (brachycephaly) and asymmetric (DP) forms of cranial deformation were scored. Interrater agreement for case status (ie, presence or absence of DP) was 93%. Exact agreement for each of the 4 severity categories was 73%. The mean of the 2 raters' ratings was used to represent the severity of each participant's cranial deformation.

Bayley Scales of Infant Development III—The Bayley Scales of Infant Development III (BSID-III)[9] yield composite scores reflecting infants' cognitive, language, and motor development. A standard score is derived for each scale, with a mean of 100 and a SD of 15. We also generated subscale scores for expressive and receptive language and fine and gross motor development, each scaled to have a normative mean of 10 and a SD of 3. Gestational age was calculated by using maternal reports of due date and birth date, and we corrected BSID-III scores for prematurity among infants born between 35 and 37 weeks of gestation and those born at 37 weeks but weighing <6 pounds. The BSID-III were administered by psychologists, physical therapists, or other trained infant psychometrists. For assessment of examiner reliability, assessments were videotaped and ~10% were reviewed independently by one of the authors (Dr Collett). Scoring agreement on individual items was ~90%.

Demographic Characteristics and Other Variables—Information on family SES and ethnicity was obtained through maternal interviews. Interviewers also asked mothers if their infants had "problems with bones, muscles, or joints (including torticollis)" that had been diagnosed by a health care provider and, if not, whether such a condition was suspected without having been formally diagnosed.

Data Analyses

We removed from further analyses case subjects with no discernible DP determined by either rater and control subjects with any degree of DP, as determined by 1 or both raters. To estimate case-control differences in neurodevelopment, we performed linear regression analyses separately for the 3 BSID-III composite scores (cognitive, language, and motor scores) and the 2 language and 2 motor subscales. We also used logistic regression to examine composite scores categorically, to determine whether more case subjects than control subjects scored below a conventional clinical threshold (ie, standard score of <85, which typically marks the developmentally delayed range of test performance). We adjusted all linear and logistic regression models for age (continuous), gender, and SES (continuous composite scores from the 4-factor classification described by Hollingshead[10]).

In secondary analyses, we compared BSID-III scores for control subjects who were rated as having mild DP with those for unaffected control subjects. Among only case subjects, we evaluated variation in BSID-III composite scores as a function of the presence or absence of torticollis and infant ages at the time of diagnosis. We conducted all statistical analyses by using Stata 10.0 (Stata, College Station, TX).

RESULTS

Study Groups

The majority of case subjects (65%) and control subjects (59%) were male (Table 1).The median age for case subjects was slightly higher (7.2 months) than that for control subjects (6.3 months). Ages for all infants ranged from 4.0 to 11.7 months. Case subjects were slightly more likely to be of white race alone (68%) and to have higher SES (72%) than were control subjects (61% and 69%, respectively). Ninety-one case subjects (39%) had been diagnosed as having torticollis, and 9 (4%) had suspected torticollis. Among control subjects, 2 (<1%) had been diagnosed as having torticollis, and 1 (<1%) had suspected torticollis.

Case Participation Bias

We compared case participants ($N = 235$) and nonparticipants ($N = 218$) with respect to 5 variables taken from medical records, that is, infant gender, age, and ethnicity; providers' ratings of DP severity (mild, moderate, or severe), on the basis of physical examination in the clinic; and family health insurance status (Medicaid versus private insurance or self-pay). Participants and nonparticipants were nearly equivalent with respect to gender (male: 65% vs 68%), age (<8 months: 91% vs 85%), severity rating (mild: 43% vs 45%; moderate: 52% vs 50%; severe: 4% vs 4%), and reimbursement category (insurance/self-pay: 79% vs 74%). Analysis of participation according to ethnicity was limited by missing data (data were unavailable for 15% of nonparticipating case subjects). Among nonparticipants for whom data were available ($n = 185$), 23% were nonwhite, compared with 32% nonwhite participating case subjects.

Severity of Deformation Among Case and Control Subjects

Two (<1%) of 235 case subjects were rated as having no DP by 1 or both dysmorphologists, and 70 (30%) of 237 control subjects were judged to have some degree of DP by 1 of the raters (Table 2). The vast majority of such control subjects (89%) were rated as having mild asymmetry.

Comparisons of Case and Control Subjects on Neurodevelopmental Measures

On average, case subjects performed worse than control subjects on all variables ($P < .001$ for all scales except the receptive language subscale, for which $P = .010$) (Table 3). For each of the 3 BSID-III scales, a greater proportion of case subjects than control subjects scored in the delayed range (Table 4). The absence of control subjects with scores of <85 on the cognitive scale precluded estimation of an odds ratio.

Secondary Analyses of Control Subjects With and Without DP

Average adjusted BSID-III cognitive composite scores for control subjects with mild or greater severity of DP were 1.4 standard score points below the adjusted scores for control subjects with no DP ($P = .385$). Adjusted language composite scores averaged 3.4 points lower ($P = .008$) and motor composite scores averaged 4.2 points lower ($P = .019$) for control subjects with DP.

Predictors of Neurodevelopment Among Case Subjects

Among case subjects, BSID-III scores were not associated with infant age at diagnosis (results not shown). There also was no association between neurodevelopment and the presence or absence of torticollis. Case subjects with and without torticollis had nearly equivalent adjusted mean BSID-III composite scores (cognitive: 102.3 vs 102.0; language: 92.8 vs 92.0; motor: 93.2 vs 93.5).

DISCUSSION

The design of this study differed from that of previous investigations in 3 ways. First, craniofacial dysmorphologists who were blinded to case status rated the head shape of every participant, including control subjects, rather than DP being diagnosed on the basis of a single practitioner's clinical judgment and it being assumed that nonreferred control subjects did not have DP. Second, in contrast to previous investigations that relied on normative test values for comparison,[2,3] we compared case subjects' test scores directly with those of a control group. The use of normative test values alone is problematic, because normative data may not adequately represent children referred to a particular clinical program, which introduces the possibility of demographic bias. Normative test values also are prone to cohort effects, which are of particular concern in research on DP because of the effects of the "Back to Sleep" campaign on infant sleep positioning and the possibility of associated increases in the prevalence of motor delays in the general population.[11–14] Normative values for instruments developed before this campaign (eg, the first and second editions of the Bayley Scales of Infant Development used in previous studies of DP) may lead to erroneous conclusions about the developmental status of an index group in relation to those normative values. Third, in addition to including control subjects, we used the BSID-III, for which normative values were established in 2004, well after initiation of the Back to Sleep campaign.

With adjustment for potential confounders, we observed differences between case subjects and control subjects on all BSID-III composite scales and subscales. The cognitive and language scale differences were clinically modest (~0.3 SD), but the motor scale composite difference was of a clinically important magnitude (nearly 0.7-SD difference favoring control group participants). This difference was more evident for the gross-motor subscale (eg, sitting up, rolling from back to side, and crawling) than the fine-motor subscale (eg, transferring objects from hand to hand). Equivalent scores were observed for case subjects with and without torticollis, which suggests that restricted neck motion did not account for the differences between case subjects and control subjects.

It is important to note that motor, language, and cognitive skills are highly correlated in early infancy, which makes it difficult to differentiate among them. For example, cognitive tasks often rely at least in part on a motor response (eg, reaching for a target stimulus). Therefore, it may be that we are detecting a fundamental motor deficit among infants with DP, which is manifested in other areas of the BSID-III because of this overlap. Follow-up assessments of this sample at later ages (currently in progress at ages 18 and 36 months) should help us to distinguish specific differences.

Despite the differences noted between case subjects and control subjects, average composite scores (range: 92–107) were near the BSID-III normative average of 100. This likely reflects the relatively low demographic risk of our sample, because both case and control families tended to have relatively high SES backgrounds (ie, ~70% of control subjects and case subjects were in the 2 highest SES categories). Similarly, although case subjects were twice as likely as control subjects to score in the delayed range of motor development (~20% and 9%, respectively), nearly 16% of the population would be expected to perform in this range on a test with standardized scores.

Our findings do not necessarily imply that DP causes neurodevelopmental delays. We have proposed several hypotheses that might account for this association,[15] although these hypotheses are tentative, untested, and an issue of some debate.[16] Possible explanations for the observed association include a direct effect of DP, in which skull asymmetry affects brain development directly, and the reverse of this situation, in which DP is a consequence rather than a cause of early neurodevelopmental delays (eg, motor impairments limit infant mobility, which promotes skull asymmetry). Unfortunately, the cross-sectional data generated here cannot distinguish these possibilities.

Blinded ratings of the 3-dimensional images confirmed DP for the vast majority of case subjects, classifying >99% of referred infants as having some degree of cranial deformation. However, the raters identified a relatively large proportion of control group participants with mildly asymmetric or flat occipital head shapes. In secondary analyses, this 30% subgroup tended to have lower BSID-III language and motor scores, compared with control subjects with no evidence of DP. We do not know how this proportion of presumably typical infants with undiagnosed DP compares with the population at large, because documented prevalence estimates have varied widely, and data from population-based studies are limited. With a birth registry sample similar to ours, Hutchison et al[17] calculated clinical cutoff scores on the basis of cephalic indices and oblique cranial length ratios and identified DP or brachycephaly in ~20% of 4-month-old infants, 9% of 8-month-old infants, and 7% of 12-month-old infants. Bias in the ascertainment of our control group might have led to an elevated rate of undiagnosed DP. During telephone screening, we explicitly queried potential control group families about head shape and excluded those whose child either had been formally diagnosed as having DP or was suspected of having DP. However, some parents might have been motivated to participate by a head shape concern that they did not mention. It also is possible that we found a high rate of undiagnosed DP because of the precision of the rating method used, which might have promoted a lower-than-usual threshold for diagnosis.

In addition to the possibility of bias in ascertainment of the control group, there might have been other sources of bias in the recruitment of both case subjects and control subjects. Among case subjects, the consent rate was relatively low (52%), which might be partly attributable to the short time frame in which families were required to participate and the clinical impression conveyed to most parents that DP is a benign craniofacial disorder, in relation to other disorders with greater morbidity (eg, craniosynostosis). We were able to assess several potential sources of bias in case ascertainment, including infant age, gender,

and ethnicity, severity of DP, and family health insurance status. These analyses provided no evidence of biased case participation. However, there might have been unmeasured sources of bias that affected our results. For example, parents with greater concern about their child's development might have been more likely to participate. To the extent that such concerns were justified, they might have contributed to overrepresentation of children with delays, compared with the general population.

Control subjects were recruited from a registry of families that agreed to be contacted for research. Although this group was similar to the case sample in terms of measured demographic characteristics, such as SES, families that participate in such a registry may differ in unquantified ways that affect infant development. To be included in the registry, parents needed to have filled out and returned a postcard within a few weeks after their infant's birth. Such parents might have had more general intellectual curiosity and greater commitment to research, and these qualities might somehow be associated with increased BSID-III scores among their children. A population cohort-based approach could address these various potential sources of bias but would require a much larger sample to ensure adequate representation of infants with significant DP.

CONCLUSIONS

The present study provides the clearest evidence to date of neurodevelopmental disadvantage among infants with DP, after adjustment for relevant sociodemographic variables. In infancy, this vulnerability seems to be most apparent in motor functions. Our continuing longitudinal follow-up study should help determine whether these observed case-control differences are persistent and whether case subjects' delays in early infancy are predictive of later outcomes. In the meantime, we recommend that pediatricians pay close attention to the motor development of infants diagnosed as having DP.

Acknowledgments

ABBREVIATIONS

DP	deformational plagiocephaly
BSID-III	Bayley Scales of Infant Development III
SES	socioeconomic status

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WHAT'S KNOWN ON THIS SUBJECT

Previous studies indicated an association between DP and compromised neurodevelopment in infancy. However, significant methodologic problems in those studies precluded definitive conclusions.

WHAT THIS STUDY ADDS

We compared case subjects with a control group, rather than comparing them only with normative test values. Experts blinded to case status rated the heads of every participant, including control subjects. We used BSID-III for evaluations.

TABLE 1

Demographic Characteristics of Infants With DP and Control Infants Without DP

Characteristic	n (%)	
	Case (N = 235)	Control (N = 237)
Gender		
Male	153 (65)	140 (59)
Female	82 (35)	97 (41)
Age		
4–5 mo	66 (28)	99 (42)
6–7 mo	107 (45)	78 (33)
8–9 mo	46 (20)	52 (22)
10–12 mo	16 (7)	8 (2)
Race/ethnicity		
White	159 (68)	145 (61)
Asian/Pacific Islander	14 (6)	13 (5)
Black	0 (0)	6 (3)
Hispanic	28 (12)	30 (13)
Mixed race/other	34 (14)	43 (18)
Familial SES		
I (high)	82 (35)	63 (27)
II	88 (37)	100 (42)
III	40 (17)	47 (20)
IV	16 (7)	21 (9)
V (low)	9 (4)	6 (3)

TABLE 2

Ratings of Severity of Cranial Deformation for Infants With DP and Control Infants Without DP

Average Severity Rating[a]	n	
	Case (N = 235)	Control (N = 237)
0	2	167
0.5	6	38
1	51	25
1.5	50	5
2	81	2
2.5	34	0
3	11	0

[a]Average severity rating from both raters. A 4-point severity scale (0 = none, 1 = mild, 2 = moderate, 3 = severe) was used to rate the overall severity of cranial deformation.

TABLE 3

Comparison of Neurodevelopmental Test Scores for Infants With DP and Control Infants Without DP

Neurodevelopmental Test	Test Score, Mean[a]		Case-Control Difference in Scores, Mean (95% Confidence Interval)[b]	P
	Case (N = 233)	Control (N = 167)		
Cognitive	102.1	107.2	−4.68 (−6.89 to −2.48)	<.001
Language (composite)	92.3	97.7	−4.96 (−6.92 to −3.00)	<.001
Receptive	8.4	9.1	−0.55 (−0.98 to −0.13)	.01
Expressive	8.9	10.1	−1.15 (−1.58 to −0.72)	<.001
Motor (composite)	93.4	103.8	−9.96 (−12.65 to −7.27)	<.001
Gross	7.6	9.9	−2.14 (−2.69 to −1.59)	<.001
Fine	10.1	11.3	−1.16 (−1.69 to −0.62)	<.001

Results were determined after removal of all case subjects rated as having no evidence of DP (severity rating of <1 from both raters) and all control subjects rated as having any DP (severity rating of 1 from either rater).

[a] Age-standardized, neurodevelopmental test scores from the BSID-III.

[b] Control subjects were used as the reference group. Values were adjusted for age (continuous), gender, and family SES10 (included as a continuous score).

TABLE 4

Comparison of Neurodevelopmental Delays (Scores of <85) for 233 Infants With DP and 167 Control Infants Without DP

Neurodevelopmental Test	Delay, n (%)		Case-Control Odds Ratio (95% Confidence Interval)[a]	P
	Case	Control		
Cognitive	9 (3.9)	0 (0.0)		
Language (composite)	43 (18.5)	17 (10.2)	1.84 (1.00–3.39)	.049
Motor (composite)	46 (19.7)	15 (9.0)	2.34 (1.25–4.39)	.008

Results were determined after removal of all case subjects rated as having no evidence of DP (severity rating of <1 from both raters) and all control subjects rated as having any DP (severity rating of 1 from either rater).

[a] Values were adjusted for age (continuous), gender, and family SES[10] (included as a continuous score)