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Original Article

Prediction of school-age IQ, academic achievement, and motor skills in children with positional plagiocephaly

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This study was approved by the Institutional Review Board at Seattle Children's Research Institute.

ABSTRACT

Introduction: Children with positional plagiocephaly and/or brachycephaly (PPB) are at risk of early developmental delay, but little is known about early life factors associated with school-age neurodevelopment. This study examined associations of demographic characteristics, prenatal risk factors and early neurodevelopment assessment with school-age IQ, academic performance, and motor development in children with PPB.

Methods: The study sample consisted of 235 school-age children with PPB followed since infancy. Outcome measures included IQ using the Differential Ability Scales-Second Edition, academic achievement as measured by the Wechsler Individualized Achievement Tests-Third Edition), and motor function using the Bruininks-Oseretsky Test of Motor Proficiency, Second Edition. Linear regression was used to examine the incremental improvement of model fit of demographics, prenatal and early life characteristics, severity of PPB, and neurodevelopment at ages 7, 18, and 36 months as measured by the Bayley-3 on school-age scores.

Results: Mean age at school-age assessment was 9.0 years. Adjusted r^2 for demographic, prenatal, and early life risk factors ranged from 0.10 to 0.22. Addition of PPB severity and Bayley-3 measures at ages 7 and 18 months did not meaningfully change model fit. Adjusted r^2 after inclusion of Bayley-3 at 36 months ranged from 0.35 to 0.41.

Conclusion: This study suggests that PPB severity and very early life neurodevelopment have little association with school-age neurodevelopment above and beyond demographic and early life risk factors. However, preschool-age neurodevelopmental assessment may still be useful in identifying children with PPB at risk for delay and who may benefit from early intervention.

Keywords: *Child development; Deformational; Infant development; Plagiocephaly; Positional*

Positional plagiocephaly and/or brachycephaly (PPB) is a common type of skull deformation, occurring in 20 to 30% of infants (1–3). While previously believed to represent a benign cosmetic condition attributed to the 'Back to Sleep' campaign, multiple studies have observed that children with PPB score lower on neurodevelopmental assessments and are at greater

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risk for neurodevelopmental delay when compared to population norms or children without PPB (4–9).

In our previous work, we observed that infants and young children with PPB scored lower on measures of cognition, early language, and motor skills than children without PPB (4,10,11). When followed into school age, these same children with PPB continued to exhibit neurodevelopmental differences relative to unaffected peers (12,13). However, differences at school age were restricted to those with moderate to severe skull deformation and unapparent in children with mild PPB. What remains unclear is whether well-known early-life indicators of neurodevelopment (e.g., socioeconomic and prenatal risk factors) (14,15), coupled with clinical characteristics of children with PPB (e.g., severity of skull deformity and infant neurodevelopmental status) are associated with school-age cognition and academic performance. Because PPB is evident in the first 12 months, identifying markers of developmental risk would have significant clinical utility for indicating the need for screening and early interventions to optimize children's longer-term outcomes.

The purpose of this study was to examine whether prenatal and clinical characteristics, including PPB severity coupled with infant/toddler neurodevelopmental assessment, are associated with the school-age developmental status of children with a history of PPB.

METHODS

Study population

This study utilized a prospective cohort design, with participants enrolled in infancy and followed into school age. We enrolled infants with and without PPB, though this analysis includes only children with a diagnosis and confirmed history of PPB.

Infants were recruited at the time of diagnosis in the Seattle Children's Craniofacial Center (see [4]). Participants were eligible if they had been diagnosed with PPB by a craniofacial specialist and were between the ages of 4 and 11 months. Infants were excluded if they (1) had a history of prematurity (<35 weeks gestation); (2) a diagnosed neurodevelopmental condition (e.g., Down syndrome), brain injury, or significant hearing or vision impairment; (3) any major malformation or ≥ 3 minor malformations; (4) craniofacial microsomia; (5) a non-English speaking mother; (6) adoption or out-of-home placement; or (7) family plans to move out of state before study completion.

The study was conducted over four time points and comprised of two main phases. Phase 1 included three assessments, with the first (Time 1) completed when children were between 4 and 11 months (age 7 months, on average) and follow-up assessments completed at ages 18 and 36 months (Times 2 and 3, respectively). Phase 2 of the study was conducted when the children were approximately 8 years of age. Informed consent was obtained from all participants and the study was approved by the Seattle Children's Hospital Institutional Review Board.

A total of 235 infants with PPB were recruited and enrolled in Phase 1. We excluded 10 of these children from Phase 2 participation and from the analyses: 2 due to a lack of discernible deformation on 3D imaging, 7 due to significant neurodevelopmental conditions diagnosed after enrolment (e.g., 22q11 deletion syndrome, Chiari malformation), and 1 due to death of the child. Two hundred and twenty-five subjects were seen at Time 1, 220 at Time 2, and 211 at Time 3. Between Phase 1 and Phase 2, 13 families could not be located, 8 declined participation, and 16 were unresponsive to outreach efforts. A total of 187 children participated in the school-aged assessment, representing 83% of those eligible.

Measures

Medical and intervention history

Information on demographic characteristics and medical history, including socioeconomic status (SES), parity, maternal age at child's delivery, and length of breastfeeding were collected at Time 1 via a semistructured interview. Information on interventions that children received (e.g., occupational or physical therapy, speech/language therapy, 'Birth to Three' services) was collected at each assessment, and information on orthotic helmet treatment for PPB was collected at Times 1 and 2.

Bayley scales of infant and toddler development, Third Edition (Bayley-3)

The Bayley-3 yields composite scores for cognitive, language, and motor development (16). Bayley-3 assessments were given by trained psychometrists at Times 1 to 3. Raw scores are converted to norm-referenced standard scores with a mean of 100 (SD=15). Bayley-3 scores were corrected for prematurity for infants born between 35 and 37 weeks gestation and those born at 37 weeks but weighing <6 pounds using gestational age. Assessments were videotaped and approximately 10% were reviewed independently by a study psychologist (BC, MS). Scoring agreement on individual items was approximately 90%.

PPB severity

Severity of cranial deformation at Times 1 and 2 were rated by 2 craniofacial paediatricians who were unaware of participants' PPB status. Three-dimensional cranial images were obtained during both study visits using the 3dMD Cranial System (see [4]). The mean of the two raters' ratings were used and rounded to whole numbers to create four ratings (none, mild, moderate, and severe); all cases with PPB were confirmed to have at least mild PPB. Inter-rater agreement was excellent for the presence/absence of deformation (κ=0.80) and good for severity rating (weighted κ=0.72). For the

purposes of this analysis, we combined moderate and severe plagiocephaly severity.

Outcomes

At Phase 2, participants completed a neuropsychological assessment battery that included measures of cognition (*Differential Ability Scales-Second Edition; DAS-2)* (17), academic achievement (*Wechsler Individualized Achievement Tests-Third Edition; WIAT-3)* (18), and motor function (*Bruininks-Oseretsky Test of Motor Proficiency, Second Edition; BOT-2)* (19). Outcomes included in this analysis included the DAS-2 General Conceptual Ability index (DAS-2 GCA), a measure of cognitive ability; a composite academic achievement score developed from the WIAT-3, calculated as an average of WIAT-3 mathematics, written expression, and total reading composites; and the BOT-2 Total Motor Composite. All measures were age- and sex-standardized. Average population normative scores are 100 (SD=15) for the DAS-2 GCA and WIAT-3 Composite Achievement scores, and 50 (SD=10) for the BOT-2 Total Motor Composite. Tests were administered by psychometrists and video recorded. Approximately 30% of tests administered were reviewed by one of the study psychologists (BC, MS) and average item level agreement ranged from 95 to 100% for the DAS-2, 94 to 100% for the WIAT-3, and 90 to 99% for the BOT-2.

Statistical analyses

Description statistics (e.g., means and standard deviations or frequencies) were calculated to compare baseline demographic and clinical characteristics in the entire sample seen at Time 1 to participants seen only at Phase 2. Because 30% of participants were missing at least one Phase 2 outcome or covariate, missing observations were imputed using the method of multivariate normal regression based on all other covariates (20). Ten imputations were performed. Linear regression with robust standard error estimates were used for all analyses. Three models were run for each of the three Phase 2 outcomes. The first model adjusted for demographic and clinical characteristics at baseline (sex, SES, race/ethnicity, gestational age at delivery, maternal age at birth, parity, and number of months the child was breastfed). The second model contained all components of Model 1 as well as PPB severity at Time 1. The third model included Models 1 and 2 as well as Bayley-3 scores using a total composite that averaged the cognitive, language, and motor development scores at Time 1, Time 2, and Time 3. We used an overall composite instead of separate Bayley-3 scores to minimize the likelihood of overfitting the models and to avoid collinearity of individual Bayley-3 scores across the different time points. An adjusted r-squared was estimated for each model iteration to evaluate overall goodness of fit and averaged across the ten imputed datasets. STATA/SE version 14.2 (College Station, TX) was used for all analyses.

RESULTS

Supplementary Table 1 provides demographic and clinical characteristics of participants with PPB in the entire sample and in participants seen only at age 8. Average age at each assessment was 7.2, 18.6, and 36.5 months for the Phase 1 visits and 9.0 years at Phase 2. Cases with PPB were predominantly male and non-Hispanic white. Seventy-five per cent of participants had moderate to severe plagiocephaly and 34% received helmet

Table 1. Associations between selected characteristics and achievement composite in children with PPB for Model 3

Characteristics	Beta	95% CI		P-value
Gender (referent=male)	−1.62	−5.44	2.20	0.40
SES	0.15	−0.03	0.33	0.10
Gestational age at delivery (weeks)	−0.44	−1.53	0.65	0.43
White race	−0.98	−5.14	3.18	0.64
Maternal age at birth	0.31	−0.08	0.70	0.12
Length of breastfeeding (months)	0.47	−0.20	1.14	0.17
Parity	0.19	−2.01	2.38	0.87
Moderate to severe PPB (referent=mild)	−2.70	−7.09	1.68	0.22
Time 1 Composite Bayley-3	−0.03	−0.34	0.27	0.82
Time 2 Composite Bayley-3	0.00	−0.21	0.22	0.97
Time 3 Composite Bayley-3	0.66	0.39	0.94	<0.001
Adjusted r^2 for all Models				
Model 1: 0.20				
Model 2: 0.21				
Model 3: 0.35				

CI Confidence interval; PPB Positional plagiocephaly and/or brachycephaly; SES Socioeconomic status.

Table 2. Associations between selected characteristics and DAS-2 GCA in children with PPB for Model 3

Characteristics	Beta	95% CI		P-value
Gender (referent=male)	1.54	−1.65	4.73	0.34
SES	0.23	0.09	0.37	0.002
Gestational age at delivery (weeks)	−0.19	−1.07	0.69	0.67
White race	−0.38	−3.85	3.08	0.83
Maternal age at birth	0.10	−0.23	0.42	0.56
Length of breastfeeding (months)	0.25	−0.30	0.80	0.37
Parity	−1.07	−2.98	0.84	0.27
Moderate to severe PPB (referent=mild)	−2.71	−6.14	0.73	0.12
Time 1 Composite Bayley-3	0.05	−0.17	0.28	0.63
Time 2 Composite Bayley-3	0.03	−0.19	0.24	0.80
Time 3 Composite Bayley-3	0.65	0.41	0.89	<0.001
Adjusted r^2 for all Models				
Model 1: 0.22				
Model 2: 0.22				
Model 3: 0.41				

CI Confidence interval; PPB Positional plagiocephaly and/or brachycephaly; SES Socioeconomic status.

therapy. Demographic characteristics were similar for Phase 2 participants and nonparticipants. Children lost to attrition were more likely to have moderate to severe plagiocephaly (89% in children lost to attrition versus 72% in children seen at Phase 2) or neurodevelopmental delay at time 3, defined as scores<85 on the Bayley-3 cognitive, language, or motor composites (19% of children lost to attrition versus 11% in children seen at Phase 2).

Data were imputed for one or more outcomes for participants missing Phase 2 outcome data (n=50, 22%), and for 59 participants (26%) who were missing data for one or more covariates. Among participants with missing data on covariates, 6% were missing PPB severity, 10% were missing Time 3 Bayley-3 scores, and 4% were missing Time 2 Bayley-3 scores.

Associations among demographic, prenatal and early life risk factors, PPB severity, and Bayley scores and outcomes at Phase 2 are presented in Tables 1–3. The beta coefficients and 95% CI presented represent those from Model 3 and the tables also include the adjusted r^2 for each of the three models. Coefficient estimates and 95% CI for Models 1 and 2 for each outcome are provided in Supplemental Tables 2–4. Adjusted r^2 for models containing demographic characteristics alone ranged from 0.10 (BOT-2 Motor Composite, Table 3) to 0.22 (DAS-2 GCA, Table 2). Although children with moderate to severe PPB at Time 1 scored lower than children with mild PPB across all three outcomes, the addition of PPB severity to the demographic, prenatal and early life characteristics included in Model 1 did not significantly improve the adjusted r^2 estimates for each model. In contrast, adjusted r^2 values improved with the addition of Bayley-3 assessments, particularly assessment at age 36 months. Overall for Model 3, the adjusted r^2 reflected that the models explained 35% of the model variability for the Achievement Composite, 41% for the DAS-2 GCA and 33% for the BOT-2 Motor Composite (Tables 1–3).

Examination of individual coefficient estimates for Model 3 show that increasing Time 3 Bayley-3 total composite scores were consistently associated with higher scores for all Phase 2 outcomes (Tables 1–3). Among demographic characteristics, SES was significantly associated with DAS GCA scores (Table 3) and male sex, which was also associated with higher BOT-2 Motor Composite scores (Table 3).

DISCUSSION

This is the first study to examine the relative importance of demographics and early-life clinical characteristics in the prediction of school-age neurodevelopment among children with PPB. While many of the characteristics studied are well-known indicators of neurodevelopment among children in general, they may be especially applicable to children with PPB, a population with known vulnerabilty to developmental delay and who are easily identifiable in infancy by parents and health care providers (6,8,9). Developmental assessments using the Bayley-3 improved the prediction of children's functioning at early school age in all outcome domains, including cognition, academic achievement, and motor functioning. While not statistically significant, moderate to severe PPB severity was associated with lower scores across all outcomes, with children with moderate to severe PPB scoring on average 2 to 3 points lower than children with mild PPB. These effect sizes are more modest than for well-known risk factors for neurodevelopmental delay such as SES (14,15,21). However, this observation is

Table 3. Associations between selected characteristics and BOT-2 Motor Composite in children with PPB for Model 3

Characteristics	Beta	95% CI		P-value
Gender (referent=male)	3.70	1.53	5.87	0.001
SES	0.00	−0.09	0.08	0.91
Gestational age at delivery (weeks)	0.00	−0.60	0.60	0.99
White race	−0.76	−2.98	1.46	0.50
Maternal age at birth	0.11	−0.11	0.33	0.33
Length of breastfeeding (months)	0.00	−0.30	0.30	0.99
Parity	0.95	−0.16	2.07	0.09
Moderate to severe PPB (ref=mild)	−1.80	−3.95	0.34	0.10
Time 1 Composite Bayley-3	−0.07	−0.21	0.06	0.29
Time 2 Composite Bayley-3	0.16	0.00	0.31	0.05
Time 3 Composite Bayley-3	0.28	0.10	0.45	0.004
Adjusted r^2 for all Models				
Model 1: 0.10				
Model 2: 0.11				
Model 3: 0.33				

CI Confidence interval; PPB Positional plagiocephaly and/or brachycephaly; SES Socioeconomic status.

nonetheless consistent with our recent findings that, in relation to unaffected controls, children who had moderate-severe PPB fare worse than those who had mild PPB (12). These findings show that while PPB severity may be associated with later neurodevelopment, early neurodevelopmental screening using an assessment like the Bayley-3 combined with knowledge of established demographic risk factors remains one of the best tools to guide identification of children who might require or benefit from closer developmental monitoring and intervention.

Our findings regarding the utility of the Bayley-3 conflict with some prior studies in other vulnerable populations where developmental measures have not been shown to predict school-age outcomes (22). For example, in a longitudinal study of extremely low birth weight infants, cognitive function at 20 months of age as measured by the BSID-II Mental Development Index performed poorly in predicting cognition at age 8 (23). A review paper by Anderson and Burnett (22) also critiqued the utility of the Bayley-3 to predict school-age academic performance, citing the tendency of the test to overestimate early neurodevelopmental skills and to underestimate the true burden of developmental delay. The authors also noted that the test performed poorly even among young children in predicting stability of skills across multiple time points. In contrast, previous work by our group in a cohort of children with single-suture craniosynostosis demonstrated that the addition of scores from the previous version of the Bayley (Bayley-2) administered at approximately 6 and 18 months of age improved the accuracy of models beyond those featuring only demographics to predict developmental delay at 36 months (24). However, the critique by Anderson and Burnett (22) is pertinent to our current study, where developmental assessments collected prior to 36 months were minimally associated with school-age outcomes. Collectively, this could suggest that older age of assessment may improve predictive validity for measures like the Bayley-3.

Strengths of the study included the use of a prospective longitudinal design, with a well-characterized cohort that has been followed since infancy. Study limitations included attrition and missing covariate data in some participants. Although overall retention in the study was good, particularly given the long follow-up interval (i.e., infancy to early school age), 22% of participants had missing data. Additional limitations included the high rate of developmental intervention in the sample (55 to 58%) and the fact that, by school age, most of the children scored within the 'average' range of test norms. In our earlier studies, when children were first observed to have developmental delays (4,10,11), we shared those results with parents and encouraged them to follow up with the child's paediatrician. These developmental interventions may have attenuated associations with school-age performance, as children who received lower developmental scores were more likely to receive services.

Clinically, these findings support the importance of assessing development in infants with PPB in order to identify those at higher risk for delay and who could benefit from early intervention. In previous papers (12,25), we have hypothesized that in the general population, the presence or absence of moderate or severe PPB might be a useful, readily observable 'marker' of developmental risk. Given the relatively high incidence of PPB in the population (as high as ~ 20%) (1–3), early intervention with these children could have substantial public health benefit in terms of the prevention or reduction of school-age learning problems. The present findings expand upon that hypothesis by suggesting that when considering only children with PPB in

the predictive equation (e.g., patients referred to a craniofacial speciality clinic), there is little value added by the precise severity of deformation; rather, demographic characteristics such as SES, and early measures of preschoolers' developmental progress may be more important from a predictive standpoint.

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