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Analysis of the correlation between deformational plagiocephaly and neurodevelopmental delay

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Summary *Background:* Deformational plagiocephaly (DP) refers to cranial asymmetry resulting from uneven external forces. A strong association exists between DP and developmental delay. We investigated the effect of DP severity on developmental delay.
Methods: Between 2010 and 2016, data from 155 patients with DP were reviewed retrospectively. Two indices were used to evaluate the deformation quantitatively: cranial index (CI) and cranial vault asymmetry index (CVAI). The Bayley Scales of Infant Development-II was used to evaluate the neurodevelopment of patients.
Results: According to the CI of the study population, 2 patients showed scaphocephaly, 12 showed mesocephaly, and 141 showed brachycephaly. For CVAI, 10 patients showed values of <3.5, 10 patients showed mild deformity (3.5—6.25), 27 patients showed moderate deformity (6.25—8.75), and 108 patients showed severe deformity. The means of the mental development index (MDI) and psychomotor development index (PDI) were 91.69 ± 16.8 and 92.28 ± 17.59, respectively; after the exclusion of patients with confounding factors, the values were 96.26 and 92.9, respectively. The Spearman correlation coefficients between MDI and CI and CVAI were -0.019662 and 0.118916, respectively, whereas for PDI, the values were -0.195428 and -0.012386, respectively.
Conclusions: There was a statistically significant neurodevelopmental delay in patients with DP. However, accelerated neurodevelopment was also encountered in many patients. MDI was found to be more affected by multiple confounding factors than PDI, whereas PDI was only

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affected by congenital anomalies. There was no definitive relationship between the severity of DP and the degree of developmental delay in our study group.
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Introduction

Although plagiocephaly may represent an underlying premature calvarial suture fusion, deformational plagiocephaly (DP) represents most cases of cranial asymmetry during infancy.[1] The major causative factor for DP is a persistent resting head position with uneven distribution of forces in the presence of malleable cranial bones and a rapidly growing brain. This persistent position does not only result in plagiocephaly but also in brachycephaly, or even in a combination of both.[2]

Recent reports have shown that cases of DP continue to increase annually, since the start of the "Back to Sleep" campaign. Furthermore, many authors reported that the incidence of DP is as high as 20% to nearly 30% among 6-month-old infants.[3–5]

However, DP may show spontaneous improvement with regard to the shape of the skull during the first 2 years of life.[6] Currently, it is widely accepted that there is a strong association between DP and developmental delay.[7,8,10] However, to date, few studies have described in detail the effect of the severity of DP on neurodevelopment and on the course of helmet therapy.

The main aims of this study were to assess the relationship between the severity of DP in Asian patients and the extent of developmental delays on presentation of patients and to compare the effects of other confounding factors on the mental and psychomotor development of patients with PD.

Methods

This study was conducted in accordance with the guidelines contained within the Declaration of Helsinki and was approved by the institutional ethics committee.

Study population

Between 2010 and 2016, patients with anthropometrically and radiologically confirmed DP at a single institution were reviewed retrospectively. Children with craniosynostosis or other skull deformities were excluded. Moreover, children with no neurodevelopmental tests either before or after treatment were also excluded.

Data were reviewed with regard to the presence of other confounding factors that might affect the neurodevelopment of the children: low birth weight (2.5 kg or lower), prematurity (<37 weeks), multiple gestation, type of delivery (vaginal vs. cesarean), intensive care admission, congenital anomaly, and syndromic disorder. We also reviewed the predisposing factors for DP, such as torticollis.

Assessment of DP severity

The head shape of the patients was routinely measured (direct anthropometry) by the senior author during the first visit. The maximal bitemporal width, antero-posterior length, both oblique diagonal lengths, and head circumference were measured.

Two indices were used for the quantitative evaluation of the head shape: (i) cranial index (CI) and (ii) cranial vault asymmetry index (CVAI). CI is defined as the ratio of the maximal bitemporal width to the antero-posterior length,[10] whereas the CVAI is defined as the ratio of the difference between the two oblique diagonal lengths divided by the larger oblique diagonal length value.[11] The patients were divided into four groups according to the CVAI: mild asymmetry (3.5–6.25), moderate asymmetry (6.25–8.75), severe asymmetry (8.75–11), and very severe asymmetry (>11).[12]

Neurodevelopmental assessment

The Bayley Scales of Infant Development-II (BSID-II) was routinely used for the evaluation of the neurodevelopment of patients. This scale yields composite scores for cognitive, language, and motor development, as well as for the parents' reports of the child's adaptive behavior. We used the mental development index (MDI) and the psychomotor development index (PDI) as the main objective scales. The patients were evaluated immediately before and after treatment by the same trained infant/toddler psychometrists. The mean results for both MDI and PDI were 100, and the standard deviations (SDs) were 15 in MDI and 16 in PDI.[13] The infants were divided into four subgroups according to the MDI and PDI scores: accelerated (SD > +1), normal (SD = −1 to +1), mildly delayed (SD = −2 to −1), and severely delayed (SD < −2).[9]

Data analysis

The Shapiro–Wilk normality test was used to analyze the patient distribution. A one-sample t-test was used to compare the MDI and PDI scores with the normative values proposed in BSID-II standardized samples for the main study group and the two smaller groups after the exclusion of patients with confounding factors. The Mann–Whitney U-test was used to investigate the effect of confounding factors, whereas Spearman correlation coefficients were used to investigate the correlation between the severity of deformation and neurodevelopmental delay. A p-value of <0.05 was considered to indicate statistical significance. For Spearman correlation, a perfect correlation was

defined when the results were +1 or −1. Data were subjected to statistical analysis with SAS version 9.2 (SAS Institute Inc., Cary, NC, USA).

Results

The study group consisted of 155 children with a confirmed diagnosis of DP (mean age, 9.9 months; range, 4—36 months) at the time of presentation. The male-to-female ratio was 106:49. The detailed demographic data of the confounding factors are listed in Table 1.

Concerning the severity of the deformities, the CI distribution was as follows: two patients showed scaphocephaly, 12 patients showed mesocephaly, and 141 patients showed brachycephaly; CI was $81 \leq 85.5$ in 24 patients and >85.5 in 117 patients. For the CVAI, the distribution of patients was as follows: <3.5 (n = 10, 6.5%); mild deformity, 3.5—6.25 (n = 10, 6.5); moderate deformity, 6.25—8.75 (n = 27, 17.4%); severe deformity, 8.75—11 (n = 29, 18.7%); and very severe deformity, >11 (n = 79, 50.9%) (see Table 2).

With regard to BSID-II, the mean of the MDI and PDI was 91.69 ± 16.8 and 92.28 ± 17.59, respectively. For the MDI, the distribution of patients was as follows: accelerated group (n = 8, 5.2%), normal group (n = 100, 64.5%), moderately delayed group (n = 37, 23.9%), and severely delayed group (n = 10, 6.5%). For the PDI, the distribution was as follows: accelerated group (n = 5, 3.2%), normal group (n = 116, 74.8%), moderately delayed group (n = 22, 14.2%), and severely delayed group (n = 12, 7.7%) (Figures 1 and 2). There were 4 patients with extreme mental and psychomotor delay (>-2 SD/score <50): 3 infants (1.9%) in the MDI test and 1 infant (0.6%) in the PDI test. Cesarean section delivery was the common confounding factor in all 4 patients, whereas premature birth was found in 2 patients, low birth weight in 1 patient, and neonatal intensive care unit (NICU) admission in 1 patient.

Analysis of the possible confounding factors in the total 155 infants revealed that the MDI score was affected by cesarean delivery (p = 0.0038), congenital defects (p = 0.0067), and intensive care unit admission (p = 0.0225), whereas the PDI score was affected only by congenital defects (p = 0.0151). The detailed data of the relation between confounding factors and neuro developmental tests are listed in Table 1.

Accordingly, patients with other confounding factors that were found to be statistically significantly affecting

Table 1   Demographic distribution of confounding factors.

Confounding factors	n (Total 155)	%
Low birth weight	35	22.5
Premature birth	29	18.7
Cesarean delivery	75	48.4
Multiple gestation	27	17.4
Congenital defect	9	5.8
Torticollis	14	9.0
NICU care	23	14.8

NICU, neonatal intensive care unit.

Table 2   Probability (p) values of confounding factors in relation to MDI and PDI.

Possible confounding factors	p-Value for MDI	p-Value for PDI
Low birth weight	0.1070	0.4799
Prematurity	0.1382	0.2273
Cesarean delivery	0.0038	0.8214
Multiple gestation	0.4673	0.3124
Congenital defects	0.0067	0.0151
Torticollis	0.8809	0.8587
NICU admission	0.0225	0.0593

MDI, mental development index; PDI, psychomotor development index; NICU, neonatal intensive care unit.

both MDI and PDI were excluded from both groups: caesarian section, congenital defects, and NICU admission in MDI, and congenital anomalies in PDI. This enabled us to correlate the severity of DP to the neurodevelopmental scales in the absence of other factors. Smaller groups composed of 69 infants for MDI and 146 infants for PDI were investigated. The means of the MDI and PDI were 96.26 and 92.9, respectively (Figures 3 and 4).

The relationship between the severity of DP and MDI and PDI showed no significance when investigated by using Spearman correlation coefficients. The 95% confidence intervals for the MDI when correlated to CI and CVAI were −0.019662 (−0.255 to 0.218) and 0.118916 (−0.121 to 0.345), respectively; for PDI, the values were −0.195428 (−0.346 to −0.035) and −0.012386 (−0.174 to 0.15), respectively.

Discussion

DP refers to cranial asymmetry and/or brachycephaly that result from uneven external forces that act on the malleable cranial bones during early infancy. Typically, patients with DP present with unilateral occipital flattening with anteriorly displaced ipsilateral ear, forehead, and cheek.[14]

Although many parents and some clinicians consider DP as a mere cosmetic problem,[15] accumulating evidence suggests that infants with DP tend to have below-average cognitive and motor development.[8,16,17]

We retrospectively reviewed data from 155 infants with DP who underwent neurodevelopmental tests. Our results showed that there was also a significant neurodevelopmental delay in our study population when compared to the BSID-II standardized samples as the means of MDI and PDI were 90.8 and 90.5, respectively. This result matched the finding of Kordestani et al., who conducted neurodevelopmental tests in 110 patients.[9] They reported that none of the infants with DP showed accelerated results. However, in our study, we encountered accelerated neurodevelopment with regard to the MDI and PDI in the pretreatment period (5.2% and 3.2%, respectively). Our results also matched the results of Speltz et al., who reported that DP does not necessarily cause neurodevelopmental delays.[18]
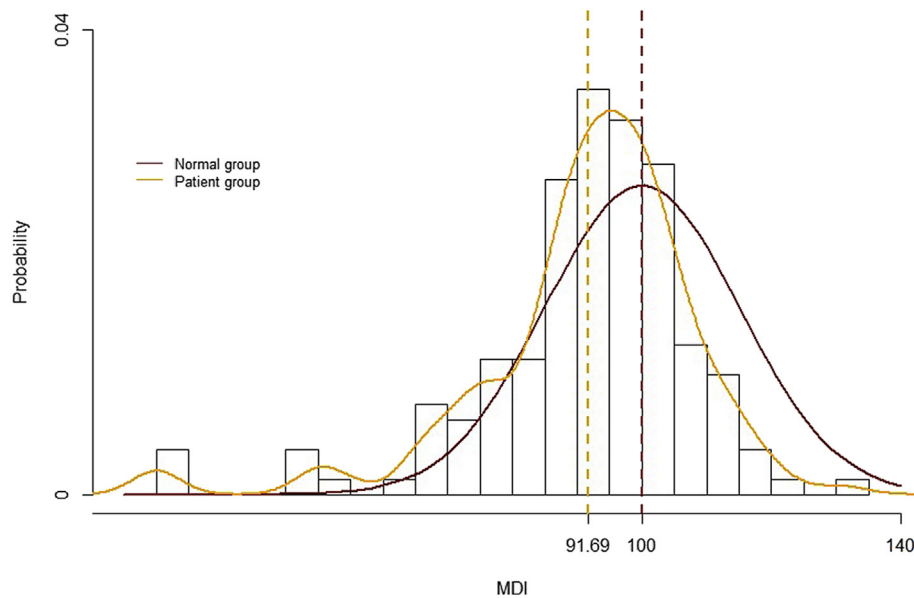
Figure 1 Histogram of the mental development index (MDI) in our study population in comparison to the normal value according to Bayley Scales of Infant Development-II. MDI mean: 91.69 ± 16.8 vs. normal: 100 ± 15 (*t*-test: p < 0.0001).
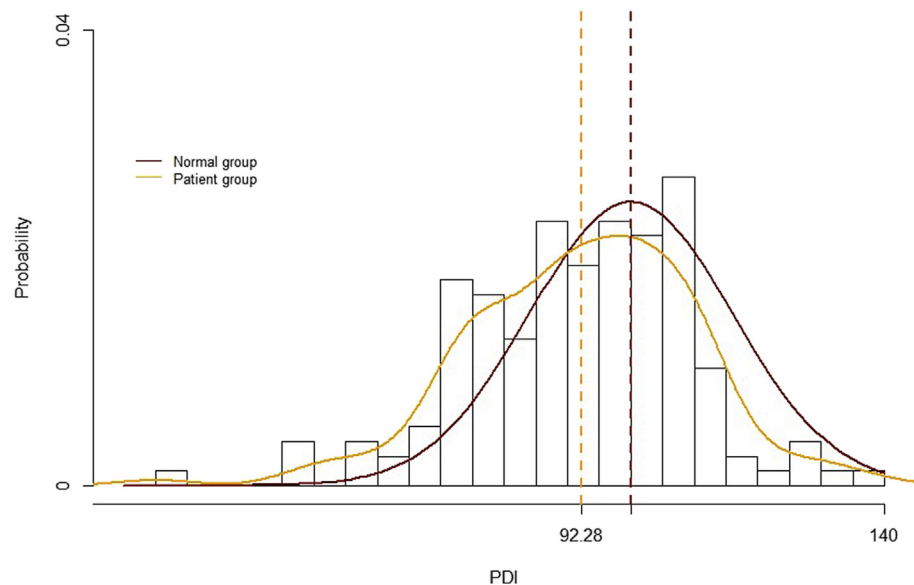

Figure 2 Histogram of the psychomotor development index (PDI) in our study population in comparison to the normal value according to Bayley Scales of Infant Development-II. PDI mean: 92.28 ± 17.6 vs. normal: 100 ± 16 (*t*-test: p < 0.0001).

The mechanisms for developmental delay and DP are still unclear. In many instances, this delay might be a consequence of preexisting medical conditions that make those infants vulnerable to DP owing to their limited mobility.[19] Accordingly, we investigated the confounding factors that might be contributing to this delay. We found that the MDI was affected by more confounding factors, including cesarean section, congenital anomalies, and early intensive care admission, whereas the PDI was affected only by congenital anomalies. This result was similar to that of Kordestani et al., who attributed the developmental delay in patients with DP to five general confounding factors: sex, low birth weight, family history, congenital

defects, and early sickness intensive care unit admission.[9] Concerning torticollis, our result was similar to the finding of Ohman et al., who reported that infants with muscular torticollis were not at a risk for developmental delay.[20] The pathogeneses for these confounding factors were described elsewhere[21] and are beyond the scope of this discussion.

Collett et al. assumed that the biomechanical effects of brain development within an asymmetric compressed skull result in alteration of the brain shape, particularly the corpus callosum and cerebellum. They reported associations between several brain shape measures and neuro-developmental outcomes, which suggest that deformation of brain structures has an adverse effect on function, even
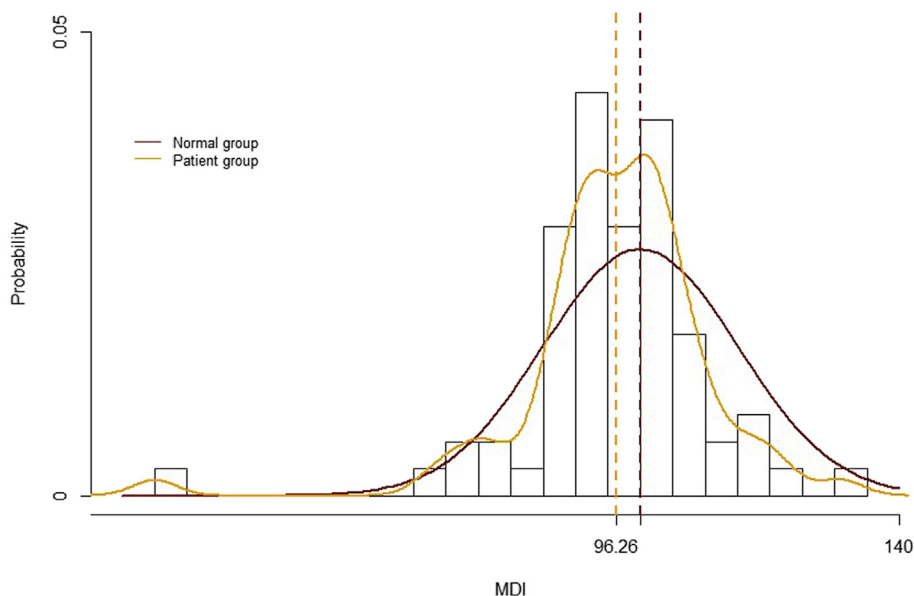
Figure 3 Histogram of the mental development index (MDI) in our study population after the exclusion of patients with confounding factors in comparison to the normal value according to Bayley Scales of Infant Development-II. MDI (N = 69) mean: 96.26 ± 14.4 vs. normal: 100 ± 15 (*t*-test: p = 0.0382).
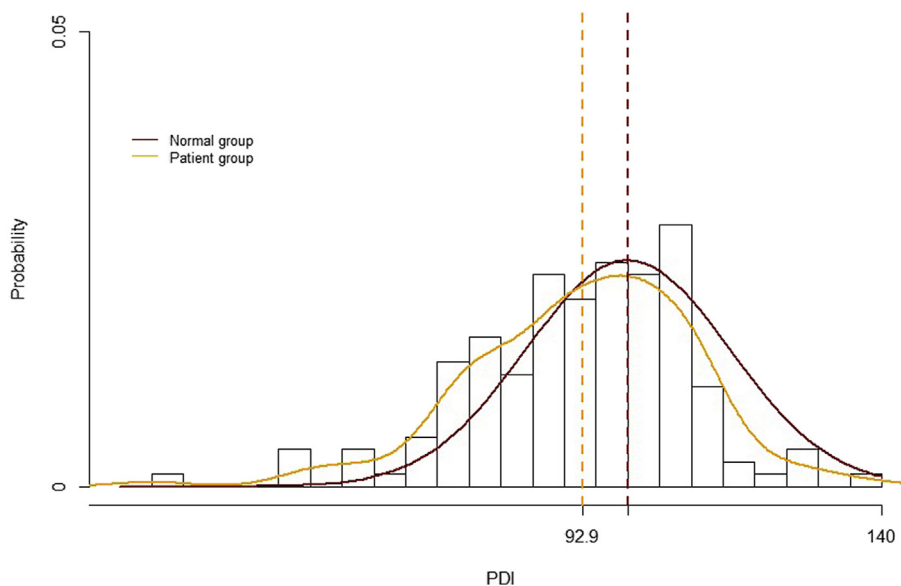

Figure 4 Histogram of the psychomotor development index (PDI) in our study population after the exclusion of patients with confounding factors in comparison to the normal value according to Bayley Scales of Infant Development-II. PDI (N = 146) mean: 92.9 ± 17.3 vs. normal: 100 ± 16 (*t*-test: p < 0.0001).

in the absence of a preexisting malformation or confounding factors.[22] Accordingly, we analyzed the effect of the severity of plagiocephaly on developmental delay. Patients who had other confounding factors that might alter the neurodevelopmental tests results were excluded, and selected groups (69 infants for MDI and 146 infants for PDI) with DP as the only condition to influence the scores were studied. The scores of these smaller groups were higher than the score of the whole study group; however, the means were still lower than the normal values provided by the BSID-II standardized samples, with statistical

significance. The results of Spearman correlation analysis between severity and neurodevelopment were surprisingly nonsignificant as we expected to see more developmental delay in patients with severe plagiocephaly.

Theoretically, the limitation of our study was the use of direct anthropometric measures for the CI and CVAI in the evaluation of severity. In addition to inter-rater variability and reliability,[23] we also hypothesize that both CI and CVAI cannot truly represent a deformed skull, which can, in turn, represent the brain shape. Another point of conflict about direct anthropometric measures was that they are strictly

linear measures and limited to a single dimension,[4] which depends on the most projecting points, whether in antero-posterior length, bitemporal width, or even oblique diagonal lengths. Thus, we recommend further objective investigations of the relationship between brain deformation and neurodevelopmental delay.

On the basis of these findings, patients with DP showed significantly lower MDI and PDI than the normal population. These values might further represent more severe delay in the presence of other confounding factors, whereas the severity of cranial vault deformation might not be related to the severity of neurodevelopmental delay. The neurodevelopmental delay in the patients in this study might be due to the alteration in the shape of the brain itself, as previously described.

Conclusion

In our study group, the means of MDI and PDI were significantly lower than the normal values for the same age/sex groups. However, accelerated neurodevelopment was also observed. MDI was found to be more affected by multiple confounding factors than PDI; the latter was affected only by congenital anomalies. We also conclude that there is no definitive relationship between the severity of DP and the degree of developmental delay in our study group.

Ethical adherence

This study was conducted in accordance with the guidelines contained within the Declaration of Helsinki and was also approved by the ethical committee "Yonsei university ethical committee, eIRB number 4-2016-0710".

Financial disclosure and products

Products that have been used in this article:

1. Analyze AVW™ (mayo clinic, USA).
2. Siemens CT scanner (Siemens Medical Solutions, Erlangen, Germany).

Disclosure

None of the authors have any conflicts of interest or financial interest in any of the products that had been used or mentioned in this article.

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