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ORIGINAL ARTICLE
Craniofacial/Pediatric

Eye and Orbital Anatomy in Metopic Synostosis

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Background: Metopic synostosis patients have a high prevalence of orthoptic anomalies, including hyperopia, astigmatism, and amblyopia. We hypothesized altered orbital anatomy contributes to suboptimal visual outcomes by adversely affecting eye anatomy and growth from early life onward. Therefore, we aimed to investigate eye and orbital anatomy in metopic synostosis.

Methods: We conducted a retrospective study in nonsyndromic metopic synostosis patients (n = 134, median age 0.43 years [IQR 0.45]) with nonsyndromic sagittal synostosis patients (n = 134, median age 0.27 years [IQR 0.23]) as controls. Primary analyses focused on eye dimensions (axial length, width, and globe height) and orbital dimensions, correcting for sex and age. Measurements were obtained from preoperative computed tomography scans.

Results: Axial length and width in metopic synostosis patients did not differ from sagittal synostosis patients, but globe height was significantly smaller ($P = 0.0002$). Lateral wall interorbital length, lateral orbital wall length, anterior medial interorbital length, and maximal medial interorbital length were significantly smaller, and anterior vertical orbital height and maximal vertical orbital height were significantly larger ($P < 0.001$). The central orbital axis and interorbital angle were significantly narrower, and medial-to-lateral orbital wall angle was wider ($P < 0.001$).

Conclusions: Metopic synostosis patients have more shallow, wider, and higher orbits. Eye dimensions are similar in sagittal synostosis patients, although globe height was smaller. Altered orbital and eye dimensions in metopic synostosis probably have a causal relation with an unknown order of development. How these dimensions relate to future orthoptic anomalies (eg, refractive error) needs further investigation. *(Plast Reconstr Surg Glob Open 2023; 11:e5303; doi: 10.1097/GOX.0000000000005303; Published online 10 October 2023.)*

INTRODUCTION

Metopic suture synostosis is caused by premature closure of the metopic suture. It is the second most common form of craniosynostosis, with an incidence of approximately one in 4500 live births.[1] The severity of the associated trigonocephaly phenotype, which includes a wedge-shaped skull and hypotelorism, ranges from a mild to severe presentation, depending on the timing of suture closure during gestation.[2]

Metopic synostosis patients are at risk for suboptimal visual outcome. Previous studies show a high prevalence of orthoptic anomalies, especially hyperopia, amblyopia, and astigmatism.[3–5] In addition, metopic synostosis patients are at risk for developing abnormal ocular movements, possibly due to altered orbital anatomy.[6] Therefore, the current craniosynostosis guideline, endorsed by the Craniosynostosis Workgroup of European Reference Network CRANIO, recommends regular ophthalmological follow-up by an ophthalmologist or orthoptist.[3,7] The underlying pathophysiology of orthoptic anomalies in metopic synostosis is unclear.

To our knowledge, only two studies investigated orbital anatomy in this population. Ezaldein et al compared orbital width, height, depth, and volume on computed

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Received for publication July 11, 2023; accepted August 11, 2023.

DOI: 10.1097/GOX.0000000000005303

Disclosure statements are at the end of this article, following the correspondence information.

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tomography (CT) scans in 23 metopic synostosis patients with 23 healthy controls aged 2–24 months. Orbital height and depth were significantly less, but there was no significant difference in orbital width or volume.[8] In contrast, Friede et al concluded that orbital width was greater in metopic synostosis patients compared with 44 cleft-lip patients but that orbital height was normal, although their sample size was limited (n = 11).[9,10]

To date, the anatomy of the eye and its relation with orbital anatomy has not been investigated in metopic synostosis. We hypothesize that eye anatomy and growth may be adversely affected by altered orbital anatomy in metopic synostosis from early life onward. Altered anatomy of the eye and orbit could potentially contribute to suboptimal visual outcomes. Therefore, we aimed to investigate eye and orbital anatomy in young metopic synostosis patients.

Takeaways

Question: Is eye and orbital anatomy altered in patients with metopic synostosis?

Findings: Using preoperative computed tomography scans, we observed more shallow, wider, higher orbits with decreased interorbital distance in metopic synostosis patients compared with sagittal synostosis patients. Eye dimensions were similar in both groups, although globe height was smaller in metopic synostosis patients.

Meaning: Altered orbital and eye dimensions in metopic synostosis likely have a causal relation with an unknown order of development. Further research is needed to determine how these altered dimensions relate to future orthoptic anomalies.

METHODS

We conducted a retrospective study at the Erasmus Medical Center, the Netherlands. No informed consent was required for the use of collected data (MEC 2016-312).

SUBJECTS

We included nonsyndromic metopic synostosis patients (no major additional congenital anomalies, major dysmorphic features, developmental delays, or neurocognitive disorders such as severe autism/behavioral disorders, and no genetic pathogenic variants causative of syndromic craniosynostosis). We included all metopic synostosis patients who underwent a craniofacial CT scan preoperatively between January 28, 2007 and August 23, 2019. We included nonsyndromic sagittal synostosis patients as controls, as they are considered to have normal orbital and eye anatomy and do not have an increased risk for orthoptic anomalies.[7,11–13] We excluded CT scans of insufficient quality to measure anatomic landmarks or CT scans with a head tilt, which made it impossible to measure anatomic landmarks. For our control group, we excluded patients with known orthoptic/visual anomalies.

CT SCAN MEASUREMENTS

Eye and orbital measurements were based on Song et al and Escaravage and Dutton, respectively.[14,15] Measurements were performed in Picture Archiving and Communications System Carestream Vue motion, version 12.2.1.4023, Carestream Health Inc, by one observer (A.E.P.). Single-eye measurements were performed on the right eye.

Eye Measurements

CT scans were angulated in a standard manner to ensure the optic nerve and lens were visible in the same axial slice. CT scans were assessed in the mediastinum window. In the axial plane, we measured axial length and axial width. In the coronal plane, we measured globe height (Fig. 1). Measurements are described in detail in Table 1.

Orbital Measurements

CT scan angulation was standardized through multiple steps and assessed in bone windows. Scans were aligned with reference to both cochlea in the axial plane. Next, scans were aligned to the middle of the infra-orbital wall in the coronal plane and the infra-orbital meatal line in the sagittal plane. In the axial plane lateral wall interorbital length, medial orbital wall length (MOWL), lateral orbital wall length, anterior medial interorbital length (AMIL), and maximal medial interorbital length (MMIL) were measured (Fig. 2A).

The following angles were measured: medial-to-lateral orbital wall angle, central orbital axis angle, and interorbital angle (Fig. 2B). In the sagittal plane, anterior vertical orbital height and maximal vertical orbital height were measured (Fig. 2C). Measurements are described in Table 1.

STATISTICAL ANALYSIS

Statistical analyses were performed using Statistical Package for Social Sciences software version 28.0.1.0(142) (IBM SPSS Statistics Inc, Chicago, Ill.) and R version4.1.3 (2022-03-10). Descriptive statistics were described as mean with SD for normally distributed continuous data and as median with interquartile range (IQR) for nonnormally distributed data. To assess if data were approximately normally distributed, we used histograms and the Shapiro-Wilk test. Parametric statistics were used if the distribution of data did not violate assumptions of normality. Groups were compared with a Welch two-sample *t* test. All measurements were investigated using scatterplots. Linear regression models were used to investigate eye dimensions with metopic synostosis/sagittal synostosis, sex, and logarithm of age as independent variables. Second, we investigated orbital anatomy differences between metopic and sagittal synostosis patients, using linear regression to correct for age and sex. To correct for multiple testing, Bonferroni correction was used. As a secondary analysis, we investigated if orbital parameters had an association with eye dimensions using linear regression models that incorporated age, sex, and all orbital parameters as independent variables. As an exploratory analysis, we

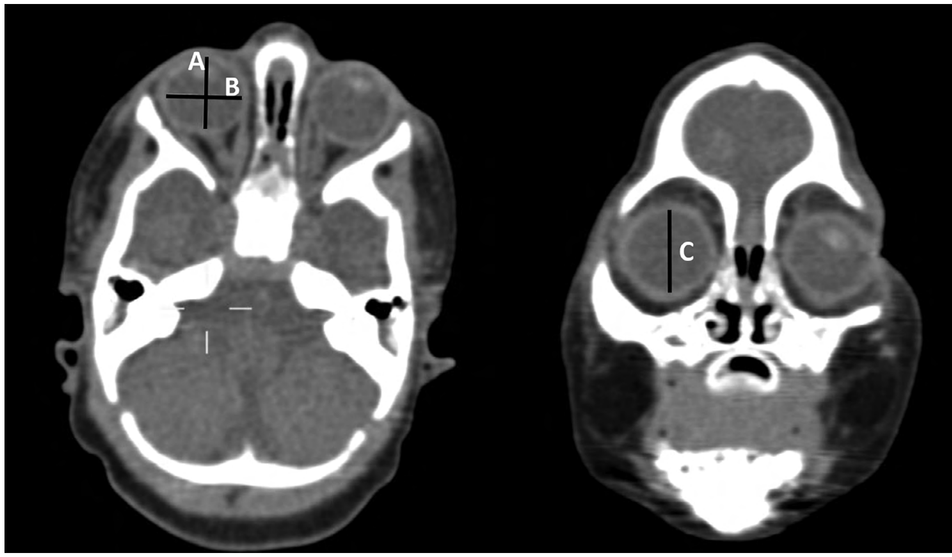

Fig. 1. Eye measurements. "A" denotes axial length; "B" indicates axial width; "C" indicates globe height.

Table 1. Eye and Orbital Anatomy Measurements with Descriptions

Eye Measurements (mm)	Description
Axial length	Distance between inner layer of the sclera and cornea, perpendicular to the center of the lens
Axial width	Distance between the widest part of the globe perpendicular to the axial length
Globe height	Vertical diameter of the eye in the coronal plane with the maximal vertical length
Orbital Measurements (mm)	**Description**
Lateral wall interorbital length	Distance between both zygomatic orbital rims
Medial orbital wall length	Anteroposterior length from the posterior lacrimal crest to the sphenoid bone
Lateral orbital wall length	Anteroposterior length from the zygomatic orbital rim to the opening of the optic canal
Anterior medial interorbital length	Distance between both posterior lacrimal crests
Maximal medial interorbital length	Maximal length between medial orbital walls
Anterior vertical orbital height	Vertical length of the orbit at the anterior edge of the orbital rim
Maximal vertical orbital height	Maximal vertical height of the orbit
Orbital Measurements (degrees)	**Description**
Medial-to-lateral orbital wall angle	Angle between medial and lateral orbital wall
Central orbital axis angle	Angle between central orbital axis and sagittal midline
Interorbital angle	Angle formed between both central orbital axes

Adapted from *Korean J Ophthalmol.* 2007;21:163–168 and *Ophthalmic Plast Reconstr Surg.* 2013;29:150–156.

assessed metopic synostosis and sagittal synostosis groups separately. Finally, we performed a secondary analysis on a subgroup of metopic synostosis patients with the most severe phenotype. Phenotypical severity was based on AMIL, MMIL, and lateral wall interorbital length, as the combination of these measurements indicates the severity of hypotelorism, one of the main phenotypical characteristics of metopic synostosis. Patients were grouped into three age groups (0–0.2 year, 0.2–0.5 year, 0.5–2 years), for which means and SDs of AMIL, MMIL, and LWIL were calculated. Patients with Z-scores less than 0 for AMIL, MMIL, and LWIL were considered to have the most severe phenotype. We used regression analyses to investigate eye dimensions with severe metopic synostosis/sagittal synostosis, sex, and logarithm of age as independent variables. Residual plots were used for all regression models to visually confirm our model's validity.

The intraclass correlation coefficient (ICC) was calculated to assess intrarater reliability by measuring 10% of CT scans in both groups by the same observer (A.P.). Another researcher (L.G.) randomly selected these CT scans. The observer and researcher were blinded to previous measurements. ICC of more than 0.75 was considered good. Measurements that did not meet this criterion were excluded from further analyses.

RESULTS

We included 268 patients, 134 craniofacial CT scans of metopic, and 134 of sagittal synostosis patients. Median age was 0.43 years [IQR 0.45] and 0.27 years [IQR 0.23] for metopic and sagittal synostosis patients, respectively ($P = 0.0003$). The male-to-female ratio was equal for both groups ($P = 0.78$; Table 2). Of the 134

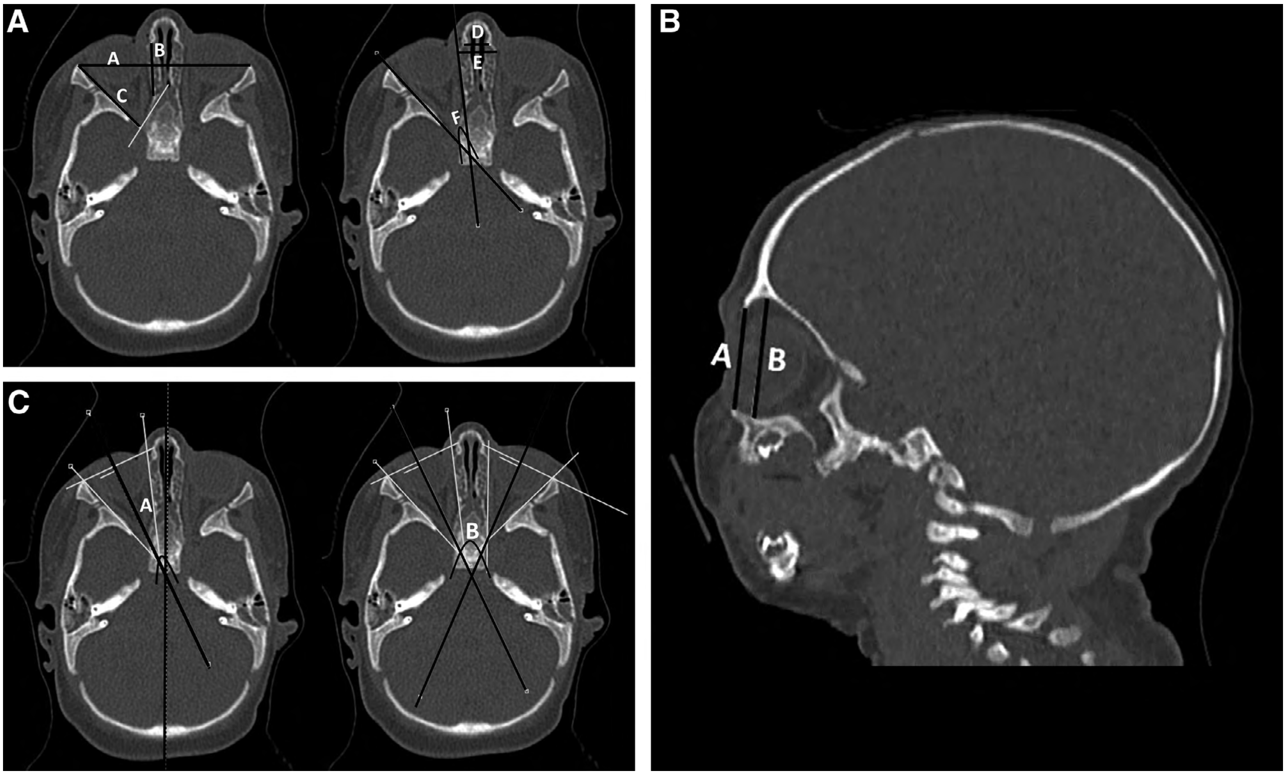

Fig. 2. Orbital measurements. A, Axial plane image illustrating five length measurements and one angle parameter: "A" indicates lateral wall interorbital length; "B," MOWL; "C," lateral orbital wall length; "D," AMIL; "E," maximal medial interorbital wall length; and "F," medial-to-lateral orbital wall angle. B, Axial plane image illustrating two angle parameters: "A," central orbital axis angle; "B," interorbital angle. C, Sagittal plane image illustrating 2 length measurements: "A," anterior vertical orbital height; "B," maximal vertical orbital height.

Table 2. Patient Demographics

Parameter	Metopic Synostosis Patients (n = 134)	Sagittal Synostosis Patients (n = 134)	*P*
Sex (male/female)	Male = 103 (76.9%) Female = 31 (23.1%)	Male = 101 (75.4%) Female = 33 (24.6%)	0.78
Median age (IQR), y	0.43 (0.45)	0.27 (0.23)	0.0003

metopic synostosis patients, 131 patients underwent surgical intervention. Three patients were considered to have a mild to moderate phenotype and were managed conservatively.

Intrarater Reliability

Most measurements had excellent intrarater reliability (ICC 0.78–1.0, $P < 0.001$; Table 3). Intrarater reliability for MOWL was poor [ICC 0.21 (–0.17 to 0.54), $P = 0.134$)]. MOWL was consequently considered unreliable and excluded from further analyses.

Table 3. Intrarater Reliability

Measurement	ICC*	95% Confidence Interval
Axial length	0.94	[0.88–0.97]
Axial width	0.91	[0.81–0.96]
Vertical height	0.87	[0.73–0.94]
Lateral wall interorbital length	1.00	[0.99–1.00]
Medial orbital wall length	0.21*	[-0.17 to 0.54]
Lateral orbital wall length	0.88	[0.75–0.94]
Anterior medial interorbital length	0.92	[0.83–0.96]
Maximal medial interorbital length	0.90	[0.80–0.95]
Medial-to-lateral orbital wall angle	0.91	[0.81–0.96]
Central orbital axis angle	0.78	[0.58–0.89]
Interorbital angle	0.85	[0.70–0.93]
Anterior vertical orbital height	0.93	[0.86–0.97]
Maximal vertical orbital height	0.98	[0.96–0.99]

*An ICC of more than 0.75 was considered good.

Eye Parameters

Scatter plots of eye dimensions are shown in Figure 3. There was no significant difference between axial length and width in metopic compared with sagittal synostosis patients, when corrected for age and sex (Table 4). Corrected for age and sex, metopic synostosis patients had significantly smaller globe heights (coefficient estimate = –0.46, 95% CI = –0.70; –0.22, $P = 0.0002$). In addition, the effect of age was significant for all eye parameters and the effect of sex was significant for axial width and globe height. Age was log-transformed to accommodate a nonlinear effect. Measurement means are provided in

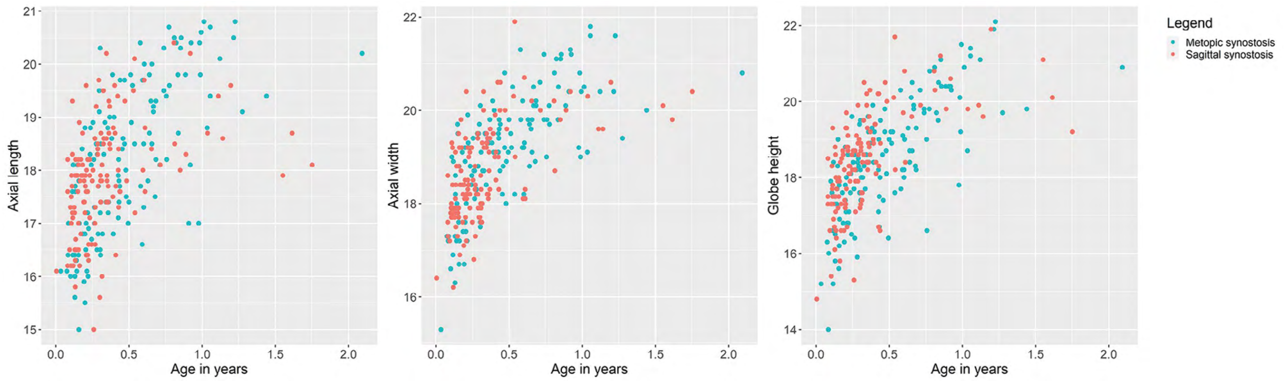

Fig. 3. Scatterplots of axial length, axial width, and globe height.

Table 4. Regression Analysis of Axial Length, Axial Width, Globe Height

	Estimate	Std. Error	*t*	*P*	95% CI
Axial length					
(Intercept)	18.99	0.17	111.98	<0.001	[18.67–19.32]
Age (log-transformed)	1.01	0.08	12.23	<0.001	[0.85–1.18]
Diagnosis (metopic synostosis/sagittal synostosis)	−0.001	0.13	−0.01	0.99	[−0.25 to 0.25]
Sex (male/female)	0.27	0.14	1.86	0.06	[−0.02–0.55]
Axial width					
(Intercept)	19.72	0.13	149.32	<0.001	[19.46–19.98]
Age (log-transformed)	1.09	0.06	16.82	<0.001	[0.96–1.21]
Diagnosis (metopic synostosis/sagittal synostosis)	0.08	0.10	0.82	0.41	[−0.11–0.27]
Sex (male/female)	0.53	0.11	4.78	<0.001	[0.31–0.75]
Globe height					
(Intercept)	19.98	0.16	123.10	<0.001	[19.66–20.30]
Age (log-transformed)	1.41	0.08	17.77	<0.001	[1.25–1.57]
Diagnosis (metopic synostosis/sagittal synostosis)	−0.46	0.12	−3.82	0.0002	[−0.70 to 0.22]
Sex (male/female)	0.43	0.14	3.16	0.002	[0.16–0.71]

Regression analysis of axial length, axial width, globe height. $P < 0.004$ considered statistically significant.

Supplemental Digital Content 1. (**See table, Supplemental Digital Content 1,** which displays the measurements of the eye and orbit. **http://links.lww.com/PRSGO/C800.**)

Orbital Dimensions Parameters

Figure 4 shows scatter plots of orbital measurements. With the exception of MOWL, all aspects of orbital anatomy of metopic synostosis patients were significantly different from sagittal synostosis patients, corrected for age and sex ($P < 0.001$; Table 5). Lateral wall interorbital length, lateral wall orbital length, AMIL, and MMIL are significantly smaller in metopic synostosis patients. Anterior vertical orbital height and maximal vertical orbital height are larger.

Orbital Anatomy Angle Parameters

Orbital angle scatter plots are shown in Figure 5. Although the central orbital axis angle and interorbital angle were significantly more narrow, the medial-to-lateral orbital wall angle was wider in metopic compared with sagittal synostosis patients (Table 5).

Association between Orbital and Eye Parameters

In an additional analysis, we investigated if there was a significant association between orbital and eye parameters using linear regression to correct for age, sex, and other orbital parameters. An increase in lateral wall interorbital length was significantly associated with an increase in the eye's axial length, and an increase in medial-to-lateral orbital wall angle was significantly associated with axial length decrease (Table 6). A positive association was found between the eye's axial width and lateral wall interorbital length. We found significant positive associations between globe height and lateral wall interorbital length, medial wall interorbital length and anterior vertical orbital height, and negative associations with AMIL, medial-to-lateral orbital wall angle and central orbital axis angle. When investigating metopic synostosis and sagittal synostosis separately, we found that LWIL had a greater effect on axial length in metopic (coefficient estimate = 0.16; 95% CI = 0.072–0.25) compared with sagittal synostosis (coefficient estimate = 0.08; 95% CI = 0.01–0.16).

EYE PARAMETERS IN METOPIC SYNOSTOSIS WITH SEVERE PHENOTYPE

In an exploratory analysis on a subgroup of metopic synostosis patients with the most severe phenotype, we identified 36 patients with Z-scores of less than 0 for

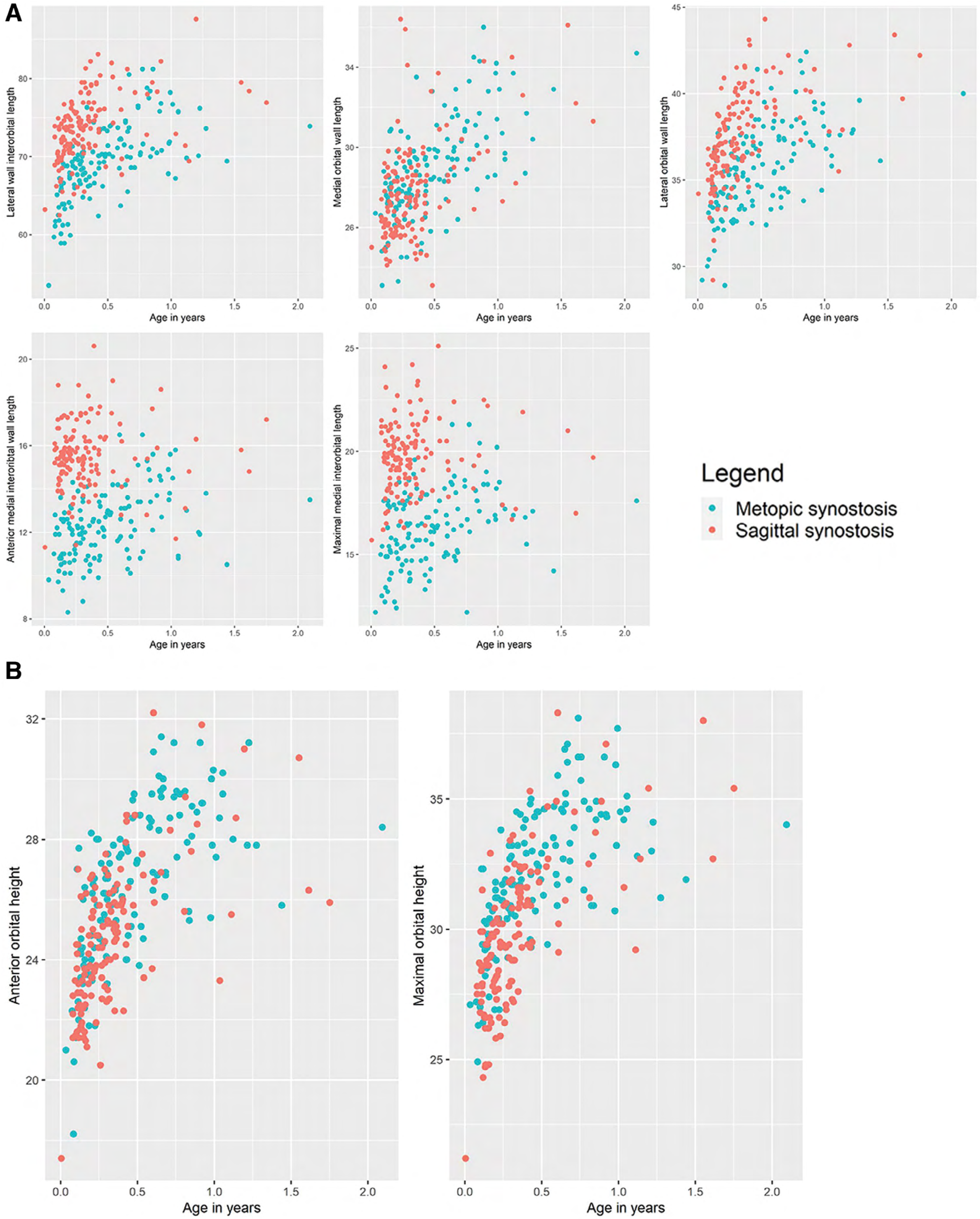

Fig. 4. Analysis of axial length, axial width, globe height. A, Scatterplots of orbital lateral wall interorbital length, MOWL, lateral wall orbital length, AMIL and MMIL. B, scatterplots of anterior orbital height and maximal orbital height.

Table 5. Orbit Dimension Regression Analyses

	Estimate	Std. Error	*t*	*P*	95% CI
Lateral wall interorbital length					
(Intercept)	77.53	0.57	134.86	<0.001	[76.40–78.67]
Age (log-transformed)	4.10	0.28	14.58	<0.001	[3.54–4.65]
Diagnosis (metopic synostosis/sagittal synostosis)	−5.93	0.43	−13.93	<0.001	[−6.77 to −5.09]
Sex (male/female)	2.18	0.49	4.48	<0.001	[1.22–3.14]
Lateral wall orbital length					
(Intercept)	39.97	0.33	119.35	<0.001	[39.31–40.63]
Age (log-transformed)	2.21	0.16	13.53	<0.001	[1.89–2.54]
Diagnosis (metopic synostosis/sagittal synostosis)	−2.73	0.25	−11.01	<0.001	[−3.22 to −2.24]
Sex (male/female)	0.69	0.28	2.45	0.015	[0.14–1.25]
Anterior medial interorbital length					
(Intercept)	16.15	0.25	64.47	<0.001	[15.65–16.64]
Age (log-transformed)	0.62	0.12	5.08	<0.001	[0.38–0.86]
Diagnosis (metopic synostosis/sagittal synostosis)	−3.46	0.19	−18.67	<0.001	[−3.83 to −3.10]
Sex (male/female)	0.26	0.21	1.25	0.21	[−0.15 to 0.68]
Maximal medial interorbital length					
(Intercept)	20.27	0.29	69.89	<0.001	[19.70–20.84]
Age (log-transformed)	0.70	0.14	4.96	<0.001	[0.42–0.98]
Diagnosis (metopic synostosis/sagittal synostosis)	−3.70	0.21	−17.24	<0.001	[−4.13 to −3.28]
Sex (male/female)	0.55	0.25	2.24	0.03	[0.07–1.03]
Anterior vertical orbital height					
(Intercept)	27.19	0.28	95.54	<0.001	[26.62–27.75]
Age (log-transformed)	2.38	0.14	17.12	<0.001	[2.11–2.66]
Diagnosis (metopic synostosis/sagittal synostosis)	0.95	0.21	4.49	<0.001	[0.53–1.36]
Sex (male/female)	0.90	0.24	3.72	0.0002	[0.42–1.37]
Maximal vertical orbital height					
(Intercept)	32.45	0.31	105.47	<0.001	[31.84–33.05]
Age (log-transformed)	2.71	0.15	18.03	<0.001	[2.42–3.01]
Diagnosis (metopic synostosis/sagittal synostosis)	1.34	0.23	5.89	<0.001	[0.89–1.79]
Sex (male/female)	1.22	0.26	4.70	<0.001	[0.71–1.74]
Medial-to-lateral orbital wall angle					
(Intercept)	39.48	0.56	70.48	<0.001	[38.38–40.58]
Age (log-transformed)	−1.18	0.27	−4.31	<0.001	[−1.72 to −0.64]
Metopic synostosis/sagittal synostosis	3.40	0.41	8.19	<0.001	[2.58–4.22]
Sex (male/female)	0.28	0.47	0.59	0.56	[−0.65 to 1.21]
Central orbital axis angle					
(Intercept)	26.11	0.41	63.69	<0.001	[25.31–26.92]
Age (log-transformed)	−1.13	0.20	−5.63	<0.001	[−1.52 to −0.73]
Diagnosis (metopic synostosis/sagittal synostosis)	−4.46	0.30	−14.68	<0.001	[−5.05 to −3.86]
Sex (male/female)	0.55	0.35	1.58	0.12	[−0.14 to 1.23]
Interorbital angle					
(Intercept)	51.96	0.74	69.88	<0.001	[50.50–53.43]
Age (log-transformed)	−2.35	0.36	−6.47	<0.001	[−3.07 to −1.64]
Diagnosis (metopic synostosis/sagittal synostosis)	−8.51	0.56	−15.46	<0.001	[−9.60 to −7.43]
Sex (male/female)	0.56	0.63	0.89	0.38	[−0.68 to 1.80]

$P < 0.004$ considered statistically significant.

AMIL, MMIL, and LWIL. We found no significant differences in axial length (coefficient estimate = 0.03, 95% CI = −0.34 to 0.40), axial width (coefficient estimate = −0.07, 95% CI = −0.37 to 0.23), or globe height (coefficient estimate = −0.22; 95% CI = −0.57 to 0.12) between patients with severe metopic synostosis compared with sagittal synostosis patients after correcting for sex and logarithm of age.

DISCUSSION

The aim of this study was to investigate eye and orbital anatomy in young metopic synostosis patients in search of an explanation for the high prevalence of orthoptic anomalies in metopic synostosis. We found that metopic synostosis patients aged 2 years or less have smaller globe heights compared with sagittal synostosis patients, although the difference was limited. There was no significant difference between axial globe length and globe width in metopic synostosis compared with sagittal synostosis patients, when corrected for age and sex. After selecting metopic synostosis patients with the most severe phenotype (N = 36), based on LWIL, MMIL, and AMIL measurements, we found no significant difference in axial length, width, or globe height compared with sagittal synostosis. Our study demonstrates that metopic synostosis patients have altered

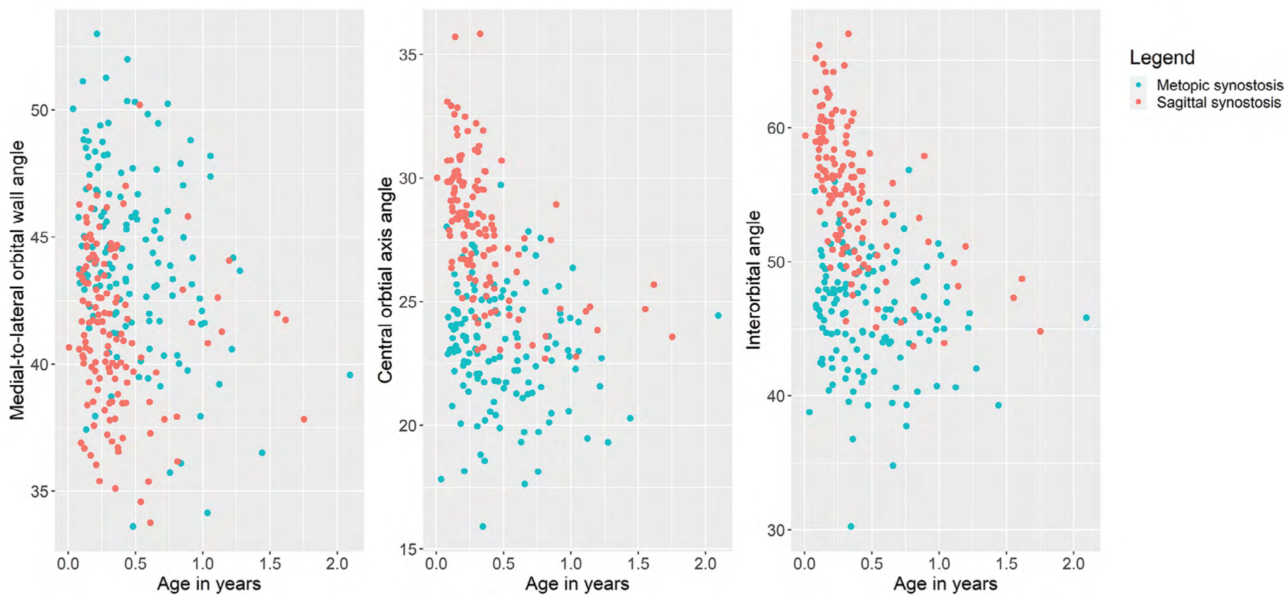

Fig. 5. Scatterplots of orbital angles.

orbital anatomy with a wider and more shallow orbit compared with our control group.

The prevalence of orthoptic anomalies, especially hyperopia, is higher in metopic synostosis patients compared with the healthy population.[3–5,11] Previous studies demonstrated a high prevalence of refractive error in both young metopic synostosis patients (24.2%[4]–28%[3] in children aged 6 years or less) and in patients who completed visual development (43.6% in patients aged 8 years or more).[5] Axial length is a major contributor to refractive error.[16] We did not find abnormal axial length or width in metopic synostosis patients aged 2 years or younger, which may be explained by a multitude of factors influencing eye dimensions and growth. First, mild hyperopia is physiological in newborns, and previous studies have shown a high prevalence of hyperopia in infants in the first year of life (7.17%–24.8%, ≥+4.00D and ≥+3.00D, respectively). The prevalence and severity of hyperopic refractive error decrease during the first year of life.[17–19] Due to a high prevalence of physiologic and true hyperopia in all infants very early in life, it is likely that the prevalence of hyperopia is similar for metopic and sagittal synostosis patients very early in infancy. The high prevalence of hyperopia early in life may have contributed to similar axial length and width, as patients in both groups aged 2 years or younger.

The eye grows fastest in the first year of life, with an increase of 1.20 mm ± 0.51 mm between the first 3–9 months of life, mostly due to vitreous chamber expansion.[17] Growth occurs rapidly until the age of 8 years, at which time the globe has reached 96% of the mean diameter of an adult-sized globe. After this age, growth is limited.[14,20] Most studies on eye dimensions are focused on axial length, and little is known about growth patterns of globe height and axial width.

Although axial globe length and width were similar in metopic and sagittal synostosis patients, our findings on orbital proportions demonstrate hypotelorism and indicate wider, more shallow orbits. Previous studies have shown that orbital growth parallels growth of the globe diameter and that the orbit has almost reached adult size at the age of 13 years.[14,21] Although studies have indicated that eye growth affects orbital growth, it is unknown to what extend altered orbital anatomy may influence the eye. Development of the metopic suture starts at 15 weeks gestational age and metopic synostosis can occur from this time point onward.[22] Depending on the timing of suture fusion, the phenotype of metopic synostosis ranges from a mild to severe phenotype with pronounced hypotelorism, temporal hollowing and a wedge-shaped forehead. We found no correlation between severity of trigonocephaly and axial globe length. Our secondary analysis suggests greater axial length in patients with larger lateral wall interorbital lengths. This distance is significantly smaller in metopic synostosis compared with sagittal synostosis patients when corrected for sex and age and will be especially small in patients with more pronounced hypotelorism. The relation between lateral wall interorbital length and axial length implies that patients with more pronounced hypotelorism have smaller axial length, which is known to contribute to hyperopia[23]. Further studies are needed to assess if lateral wall interorbital length affects axial globe length development or vice versa, and if the severity of trigonocephaly is associated with refractive error.

In addition to a wider more shallow orbit, our results indicate a higher orbit as both anterior and maximal vertical orbital height were significantly greater in metopic synostosis. In contrast, at this age, globe height was smaller. Metopic synostosis patients have a teardrop-shaped orbit. This could potentially explain the contradictory results of orbital and eye dimensions. In teardrop-shaped eyes, the maximal orbital vertical height is measured more anteriorly and medially, while the globe is located at the center of the orbit and does

Table 6. Association between Orbital and Eye Parameters Using Regression Analyses

	Estimate	Std. Error	*t*	95% CI
Axial length				
(Intercept)	10.68	1.77	6.03	[7.19–14.17]
Age (log-transformed)	0.24	0.14	1.69	[−0.04 to 0.53]
Diagnosis (metopic synostosis/sagittal synostosis)	0.41	0.23	1.82	[−0.03 to 0.86]
Sex (male/female)	−0.04	0.14	−0.31	[−0.33 to 0.24]
Lateral wall interorbital length	0.12	0.03	4.29	[0.07–0.18]
Lateral wall orbital length	−0.01	0.04	−0.28	[−0.09 to 0.06]
Anterior medial interorbital length	−0.01	0.05	−0.20	[−0.11 to 0.09]
Maximal medial interorbital length	−0.07	0.05	−1.58	[−0.16 to 0.02]
Medial-to-lateral orbital wall angle	−0.05	0.02	−2.72	[−0.09 to −0.01]
Central orbital axis angle	−0.01	0.05	−0.28	[−0.12 to 0.09]
Interorbital angle	0.003	0.03	0.09	[−0.06 to 0.06]
Anterior vertical orbital height	0.05	0.05	1.18	[−0.04 to 0.14]
Maximal vertical orbital height	0.05	0.04	1.24	[−0.03 to 0.14]
Axial width				
(Intercept)	10.68	1.34	7.94	[8.03–13.32]
Age (log-transformed)	0.49	0.11	4.50	[0.28–0.71]
Diagnosis (metopic synostosis/sagittal synostosis)	0.47	0.17	2.74	[0.13–0.81]
Sex (male/female)	0.26	0.11	2.38	[0.05–0.47]
Lateral wall interorbital length	0.11	0.02	5.01	[0.07–0.15]
Lateral wall orbital length	0.01	0.03	0.43	[−0.05 to 0.07]
Anterior medial interorbital length	−0.003	0.04	−0.09	[−0.08 to 0.07]
Maximal medial interorbital length	−0.04	0.04	−1.19	[−0.11 to 0.03]
Medial-to-lateral orbital wall angle	−0.0002	0.01	−0.01	[−0.03 to 0.03]
Central orbital axis angle	0.03	0.04	0.74	[−0.05 to 0.11]
Interorbital angle	−0.02	0.02	−1.02	[−0.07 to 0.02]
Anterior vertical orbital height	0.04	0.03	1.13	[−0.03 to 0.11]
Maximal vertical orbital height	0.01	0.03	0.37	[−0.05 to 0.08]
Globe height				
(Intercept)	11.83	1.63	7.25	[8.62–15.04]
Age (log-transformed)	0.64	0.13	4.83	[0.38–0.90]
Diagnosis (metopic synostosis/sagittal synostosis)	−0.43	0.21	−2.05	[−0.84 to −0.01]
Sex (male/female)	0.15	0.13	1.17	[−0.11 to 0.41]
Lateral wall interorbital length	0.07	0.03	2.66	[0.02–0.12]
Lateral wall orbital length	0.01	0.04	0.26	[−0.06 to 0.08]
Anterior medial interorbital length	−0.11	0.05	−2.47	[−0.20 to −0.02]
Maximal medial interorbital length	0.04	0.04	0.99	[−0.04 to 0.13]
Medial-to-lateral orbital wall angle	−0.03	0.02	−1.80	[−0.07 to −0.003]
Central orbital axis angle	−0.11	0.05	−2.28	[−0.21 to −0.02]
Interorbital angle	0.05	0.03	1.61	[−0.01 to 0.10]
Anterior vertical orbital height	0.16	0.04	3.77	[0.08–0.24]
Maximal vertical orbital height	0.02	0.04	0.62	[−0.05 to 0.10]

not fully extend to the maximal orbital vertical height (Fig. 1). Although the globe height difference was statistically significant, there has been little research on globe height, making it difficult to interpret this limited difference and its relevance to hyperopia.

Finally, we investigated associations between eye and orbit in a secondary analysis. Axial length was associated negatively with medial-to-lateral orbital wall angle. This indicates that patients with shorter axial globe length had wider orbits. Although axial globe length is not significantly different in metopic synostosis compared with sagittal synostosis patients early in life, the wider medial-to-lateral orbital wall angle could potentially contribute to developing a shorter axial globe length during growth. In contrast, we failed to find a significant association between axial globe length and lateral wall orbital length, although we did not have sufficient statistical power to investigate associations between eye and orbital dimensions fully.

Our study has several limitations. First, our control group consisted of sagittal synostosis patients rather than patients without skull deformities. However, to our knowledge, sagittal synostosis does not affect the orbits, and these patients do not have an increased risk of orthoptic anomalies. In addition, the axial globe length and width we measured is comparable to axial length in healthy controls. Lim et al researched eye size and shape in newborn Asian children aged 5–17 days. Mean axial globe length was 17.3 ± 0.9 mm and mean axial width 16.3 ± 0.8 mm.[24] Especially axial globe length is similar to the mean axial globe length in sagittal synostosis patients. The small difference between groups could be explained by age differences between patients in our study compared with children included by Lim et al, different measurement instruments, and different ethnicity.

Second, there was a significant difference between the age of metopic and sagittal synostosis patients. We corrected for this in our analyses. Finally, although most measurements had a good ICC, the ICC of MOWL was poor [0.21, (−0.17 to 0.54)]. It was difficult to establish the defined anatomic landmarks for MOWL and align them in the same plane, possibly because the skull was not fully developed at the time of measurement.

FUTURE RECOMMENDATIONS

Based on our results, we hypothesize that persisting abnormal orbital dimensions could potentially mechanically alter eye dimensions and contribute to orthoptic anomalies in metopic synostosis. This further underlines the importance of the recommended regular screening for orthoptic and visual anomalies in patients with metopic synostosis throughout the course of life, as early detection and treatment of these anomalies is key to optimize visual outcome.[7] Future studies should assess if altered orbital dimensions persist after the eye and orbit have fully developed and if there is any relation with orthoptic anomalies. It would be preferred to investigate orbital and eye dimensions without further radiation exposure in childhood, which may be possible given the advances in radiological imaging and introduction of magnetic resonance imaging sequences able to visualize bone structures.

In addition, there is an ongoing debate on if metopic synostosis patients should be operated on or managed conservatively. Few studies have researched the effect of surgery on visual outcome.[3,25,26] Denis et al concluded that postponing surgery until after the age of 6–7 months may result in a higher risk of astigmatism and strabismus, although they only investigated eight metopic synostosis patients.[25,26] A second study investigating 14 trigonocephaly patients also suggested later surgery resulted in more pronounced astigmatism. MacIntosh et al contradicted these results. They investigated 64 metopic synostosis patients, of whom 57 underwent cranial vault surgery after the age of 12 months. They found no significant difference in refractive error and found the highest incidence of refractive error and squint in patients who underwent surgery before the age of 12 months (N = 7).[3] Given these conflicting results and limited sample sizes, the effect of surgery on visual outcome should be investigated further and be compared with conservative management.

CONCLUSIONS

In conclusion, metopic synostosis patients have altered orbital dimensions that indicate more shallow, wider, higher orbits with decreased interocular distance compared with sagittal synostosis patients. The height of the eye was smaller, although the difference was small. In contrast, axial globe length and width are similar in metopic and sagittal synostosis patients very early in life.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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