Received: 10 September 2023 | Accepted: 6 November 2023

DOI: 10.1111/aos.15814

Acta Ophthalmologica

ORIGINAL ARTICLE

Central macular morphology and optic nerve fibre layer thickness in young adults born premature and screened for retinopathy of prematurity

Dýrleif Pétursdóttir[1,2] | **Hanna Åkerblom**[1,3] | **Gerd Holmström**[1] | **Eva Larsson**[1]

[1]Department of Surgical Sciences/Ophthalmology, Uppsala University, Uppsala, Sweden

[2]Department of Ophthalmology, Faculty of Medicine, National University Hospital, University of Iceland, Reykjavík, Iceland

[3]Centre for Clinical Research Västmanland, Hospital of Västmanland, Västerås, Sweden

Correspondence
Dýrleif Pétursdóttir, Department of Surgical Sciences/Ophthalmology, Uppsala University, S-75185 Uppsala, Sweden.
Email: dyrleif.petursdottir@uu.se

Funding information
Ögonfonden; Synskadades vänner i Uppsala län; The Carmen and Bertil Regner Foundation; The Crown Princess Margaretha Foundation for the Visually Impaired

Abstract

Purpose: To investigate central retinal morphology and optic retinal nerve fibre layer (RNFL) in prematurely born young adults and compare to term born controls.

Materials and Methods: The participants were 59 prematurely born individuals, with a birthweight ≤1.500 g, and 44 term born controls, all 25–29 years of age. Visual acuity (VA) and contrast sensitivity (CS) were assessed. The retinal macular thickness, ganglion cell-inner plexiform layer (GC-IPL) thickness and RNFL thickness were assessed with Cirrus optical coherence tomography (OCT).

Results: Central macular thickness was increased (mean 26.7 µm) in prematurely born individuals compared to controls. The macular GC-IPL was thinner (mean 3.84 µm), also when excluding those with previous retinopathy of prematurity (ROP) and those with neurological complications. Gestational age at birth and previous treatment of ROP were risk factors for a thicker macula, however, not for reduced GC-IPL. The average peripapillary RNFL was thinner (mean 4.61 µm) in the prematurely born individuals, also when excluding those with previous ROP and/or neurological complications. Within the prematurely born group, treated ROP was correlated with increased average RNFL. Further, both better VA and CS were associated with thinner optic nerve RNFL and thicker average GC-IPL.

Conclusion: Macular and optic nerve morphology were influenced by premature birth as assessed with OCT in adult individuals. Gestational age at birth and treatment for ROP seemed to affect central macular thickness, and treated ROP affected the peripapillary RNFL. Thus, retinal sequelae remained in adulthood.

KEYWORDS
ganglion cell-inner plexiform layer (GC-IPL), macular thickness, optical coherence tomography (OCT), prematurity, retinal nerve fibre layer (RNFL), retinopathy of prematurity (ROP)

1 | INTRODUCTION

Premature birth can affect the prematurely born individual in many ways. Ocular sequelae include retinopathy of prematurity (ROP), which is one of the main neonatal morbidities following preterm birth (Express Group, 2010). It is a neurovascular disorder, characterized clinically by abnormal retinal vascular development (Hellström et al., 2013). However, even without ROP, premature birth has been shown to influence the development of the retina, including the fovea (Akerblom et al., 2011; Molnar et al., 2017). The fovea starts to develop at 12 weeks gestational age (GA); after mid-gestation, there is centrifugal displacement of the inner retinal cells to begin formation of the optic pit; and after term, a centripetal displacement of photoreceptors takes place to increase the foveal cone density. Cone density increases from birth until 15 months

of age, when cone elongation begins and continues until around 13 years (Hendrickson et al., 2012; Provis et al., 1998). Central macular thickness and persistence of inner retinal layers are examples of foveal changes that have been associated with premature birth (Yanni et al., 2012).

Premature birth has been shown to influence the development of the central nervous system as well (de Kieviet et al., 2012; Saigal & Doyle, 2008). The retinal nerve fibre layer (RNFL) develops from the optic nerve and is part of the central nervous system. Studies on prematurely born children and adults have shown a thinner RNFL in the eyes of prematurely born individuals (Akerblom et al., 2012; Fieß, Schäffler, et al., 2022). This seems to be related to the brain structure and neurodevelopment (Rothman et al., 2015).

We have previously reported on the influence of premature birth on the visual function of a well-defined population of prematurely born young adults (Pétursdóttir et al., 2020). The aim of this study was to investigate the central retinal morphology in the same cohort and compare to term born controls.

2 | MATERIALS AND METHODS

2.1 | Participants

This study is part of a larger longitudinal, population-based follow-up study on the ophthalmological outcome of prematurely born individuals who were screened for ROP in the neonatal period and treated with cryotherapy when indicated. The prematurely born individuals were all part of a population-based study on the incidence of ROP, and thereafter took part in ophthalmological follow-up from 6 months until 10 years of age. Fifty-nine prematurely born individuals participated. They were born in Stockholm County, Sweden, between 1 November 1988 and 31 October 1990, with a birthweight (BW) of ≤1500 g. Forty-four controls were born at term in the same area, at the same time period, and with normal BWs. The criterion for ROP treatment in Sweden at that time was ROP stage 3 in at least four clock hours in zone II, with or without plus disease (Holmstrom et al., 1993). The study group was divided according to the degree of ROP in the neonatal period, that is, no ROP, untreated ROP, and treated ROP. At 2.5 years of age, neurological complication was defined as intraventricular haemorrhage grade 3 or 4 in the neonatal period and/or obvious neurologic sequelae (epilepsy, cerebral palsy or mental retardation) (Holmstrom et al., 1993, 1999; Holmstrom & Larsson, 2008).

Previous reports from the follow-up describe the study subjects as well as the control group in more detail (Pétursdóttir et al., 2020, 2021, 2022a, 2022b).

The study was conducted according to the Declaration of Helsinki and approved by the regional Ethical Review Board of Uppsala, Sweden (Dnr 2014/584). All participants signed a written consent before participation.

2.2 | Methods

Best-corrected distance visual acuity (VA) was assessed monocularly with the logarithmic Early Treatment Diabetic Retinopathy Study Research Group (ETDRS) (1985) chart at 4 m and contrast sensitivity (CS) with the Vistech Contrast Sensitivity Test System (VCTS 6500) (Vistech Consultants, USA). Contrast sensitivity was calculated as area under the curve (AUC) and has been described elsewhere (Pétursdóttir et al., 2020). Refraction in cycloplegia was assessed and spherical equivalent calculated.

Optical Coherence Tomography (OCT) scans were acquired using the spectral domain Cirrus HD-OCT 4000 (Carl Zeiss Meditec, Dublin, CA). The scans were performed through dilated pupils, and a single scan with signal strength ≥6 was selected for further analysis.

The Macular Cube scan 512 × 128, covering 6 × 6 mm of the retina with the fovea centred, was used for imaging the macular structure. The average retinal thickness was presented as numeric values for nine macular areas defined by the ETDRS Research Group (1). The central region is 1 mm in diameter (A1), the inner and outer circles are divided into four quadrants each, A2–A5 and A6–A9. The cube average thickness in micrometres and the total macular volume (cup volume, CV) in square millimetres were also noted. Furthermore, the ganglion cell-inner plexiform layer (GC-IPL) analysis segmentation algorithm was used to present the thickness of individual sectors of the macula superotemporal (ST), superior (S), superonasal (SN), inferonasal (IN), inferior (I), inferotemporal (IT), together with the average and minimum GC-IPL.

The RNFL thickness was measured with the Optic Disc Cube 200 × 200 protocol, and the average RNFL thickness and the RNFL thickness in different quadrants (S (superior), N (nasal), I (inferior) and T (temporal)) recorded.

2.3 | Statistical methods

Data are described descriptively using absolute frequencies for categorical variables and mean, standard deviation and range for numerical variables. Comparison between prematurely born and controls was performed using linear mixed models where all models included fixed effects of group, sex and refraction and subject number as random factors, taking into account repeated measures within subject (left and right eye). Results from mixed models are presented as estimated mean difference between groups with 95% confidence interval and *p*-value.

To explore risk factors regarding central macular thickness and RNFL within the prematurely born group, GA, BW, sex, neurological complications, ROP and treated ROP, were evaluated with univariable and multivariable linear mixed models.

No adjustments for multiplicity have been performed; thus, all *p*-values should be interpreted with that in mind.

3 | RESULTS

Fifty-nine prematurely born individuals and 44 full-term controls, all 25–29 years of age, participated in the study, see Table 1. One of the prematurely born individuals could not participate in the OCT assessments due to severe autism. This individual had no ROP in the neonatal period. Further, it was only possible to achieve good quality readings from the left eye of one prematurely born, because of very poor vision in the right eye. All 44 controls could complete the OCT assessments in both eyes. The outcome of logMAR VA, CS and refraction in the prematurely born and control groups have been described previously (Pétursdóttir et al., 2020, 2022a, 2022b).

The macular thickness in the nine EDTRS areas (A1-A9) are reported in Figure 1. The central area (A1) was significantly thicker (26.7 μm) in the prematurely born individuals compared to controls ($p<0.001$), see also Figure 2. The ones without ROP had a mean thickness in A1 of 281 (SD 20) μm in the right eyes (REs) and 283 (SD 20) μm in the left eyes (LEs), and the ones with untreated ROP had a mean value of 281 (SD22) μm in the REs and 280 (SD 24) μm in the LEs. The formerly treated children had the thickest central area, 296 (SD 26) μm in the REs and 303 (SD 29) in the LEs. The difference remained when excluding individuals with previous ROP, including treated ROP, and individuals with a neurological complication according to our definition ($p<0.001$). There was no difference in the other macular areas nor the inner and outer circle of macula, see Figure 2. No difference was found in the total macular volume between prematurely born individuals and controls (REs 10.2 (SD 0.50), LEs 10.27 (SD 0.52) versus REs 10.34 (SD 0.47), LEs 10.35 (SD 0.48)).

The ganglion cell layer thickness in the six macular areas as well as average are given in Figure 3. The mean difference between prematurely born individuals and controls in the areas ranged from 3.1–4.8 μm, and the GC-IPL was statistically thinner in preterms in all areas ($p<0.05$), see Figure 3. The average GC-IPL was, in mean, 3.84 μm thinner in prematurely born individuals ($p<0.05$) compared to controls and the minimum GC-IPL 8.02 μm thinner ($p=0.001$). The statistical difference between preterms and controls remained after excluding those with previous ROP, including treated ROP, and those with previous neurology ($p<0.05$ and $p<0.01$).

Regarding optic nerve head OCT, the RFNL in the superior, inferior, temporal and nasal sectors together with the average RNFL thickness are given in Table 2 and Figure 4. The average RNFL thickness was significantly thinner in prematurely born individuals compared to controls, and in the inferior and nasal sectors of the optic nerve head, see Table 2. However, when excluding those with previous neurology according to our definition, and those with previous ROP (including treated ROP), the significant difference remained only regarding the average RNFL (difference −5.38, confidence interval (CI) −9.47 to −1.29, $p<0.05$) and the nasal sector (difference −9.57, CI −14.75 to −4.39, $p<0.01$).

Within the prematurely born group, risk factors such as gestational age (GA), BW, sex, neurology, ROP and treated ROP, were evaluated with univariable and multivariable analyses. The statistically significant results from the multivariable analyses of the risk factors are presented in Table 3. The central macular thickness (A1) decreased by 3.65 μm with every additional week of GA, also illustrated in Figure 5, that is, low GA was a risk factor for thicker macula. Previous treatment of ROP was a risk factor for thicker central macula ($p=0.05$), Table 3. Regarding the ganglion cell layer in the macula, no significant risk factors were found for reduced thickness. Treated ROP was found to be a risk factor for increased average RNFL, Table 3, which was most obvious in the temporal sectors, see Figure 4.

Within the prematurely born group, we also analysed the correlations between VA and CS (AUC) with the OCT measurements. The central macular thickness (A1) was not associated with VA nor CS. In multivariable analyses, thicker average GC-IPL was associated with

TABLE 1 Demographics of prematurely born individuals and controls.

	N RE/LE	Gender M/F	GA at birth (w) Mean (SD) Range	BW (g) Mean (SD) Range
Controls	44/44	26/18	39–41 N/A	3000–4000 N/A
Prematures	59/59	22/37	29 (2) 24 to 34	1167 (237) 700 to 1490
No ROP[a]	34/36	16/18	30 (2) 26 to 34	1264 (195) 711 to 1490
Untreated ROP[a]	12/10	4/8	29 (2) 27 to 32	1082 (258) 750 to 1466
Treated ROP[a]	13/13	2/11	28 (2) 24 to 32	993 (201) 700 to 1380

Abbreviations: BW, birth weight, f, female, g, grams, GA, gestational age, L, left eye, m, male, N, number, n/a, not applicable, RE, right eye, ROP, retinopathy of prematurity, SD, standard deviation, w, weeks.

[a]In the eye with the most severe stage of ROP.

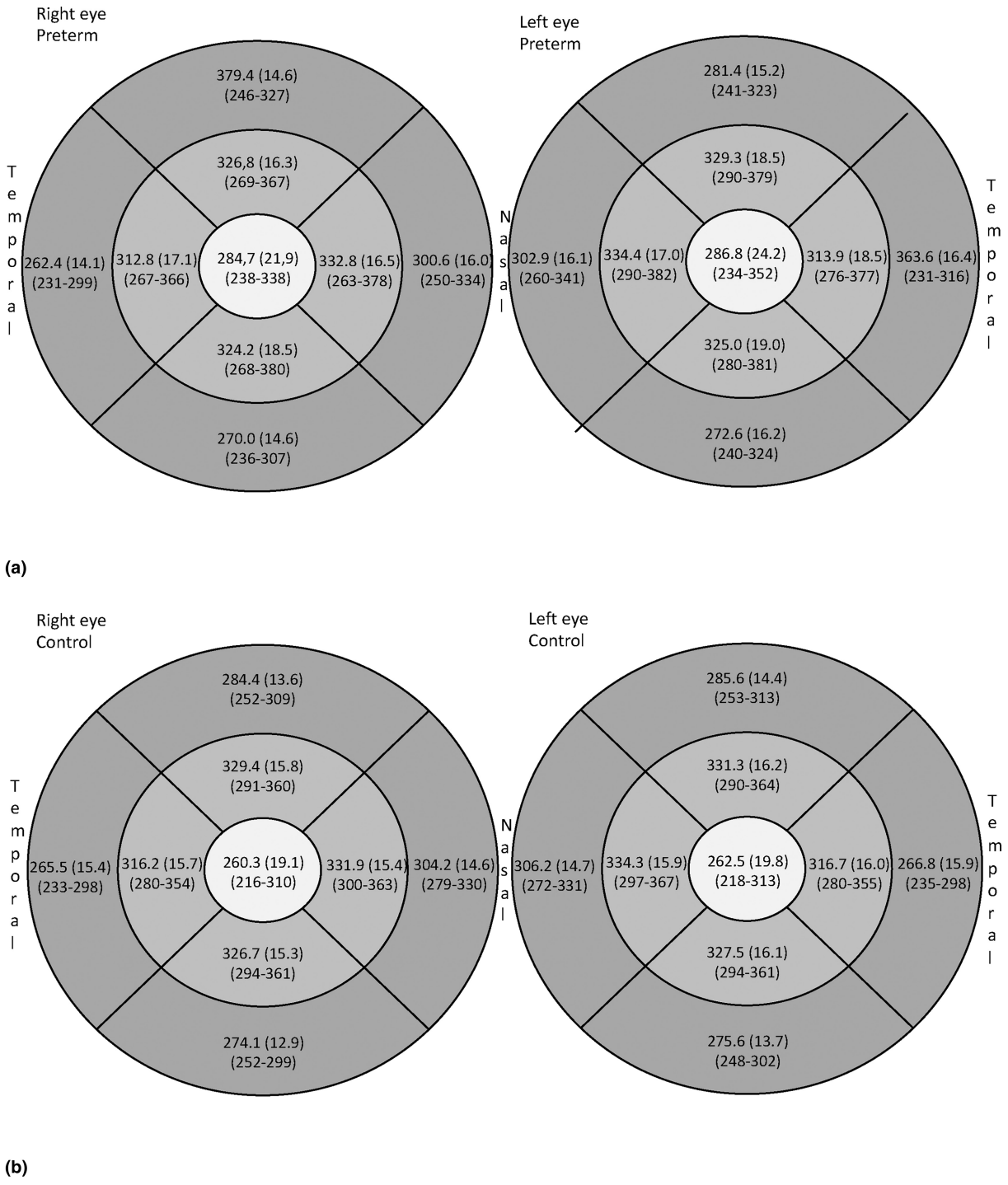

FIGURE 1 (a, b) Retinal thickness (μm) in the nine Early Treatment Diabetic Retinopathy Study areas, mean (standard deviation) and range. (a) Preterm group right and left eyes. (b) Control group, right and left eyes.

better logMAR VA (−0.0049, CI −0.0074 to −0.0025, $p<0.001$), see Figure 6, and better CS (0.0061, CI 0.0021 to 0.0101, $p=0.005$). Thicker RNFL was correlated with worse logMAR VA (0.0042, CI 0.0019 to 0.0065, $p=0.001$) and worse CS (−0.0058, CI −0.0098 to −0.0017, $p=0.007$).

4 | DISCUSSION

In the present study, retinal morphology was assessed with OCT in prematurely born individuals in adulthood, who had been screened for ROP, and compared with individuals born at term. We found that the central macular thickness was increased in individuals born preterm and that the macular ganglion cell layer was thinner, also when excluding those with previous ROP and those with neurological complications. Gestational age at birth and previous treatment of ROP were risk factors for a thicker macula, however, not for reduced GC-IPL. The average peripapillary RNFL was found to be thinner in the prematurely born individuals, also when excluding those with previous ROP and those with neurological complications. Within the prematurely born group, treated ROP was a risk factor for increased average RNFL. Further, both better VA and CS were associated with thinner optic nerve RNFL and thicker average GC-ILP.

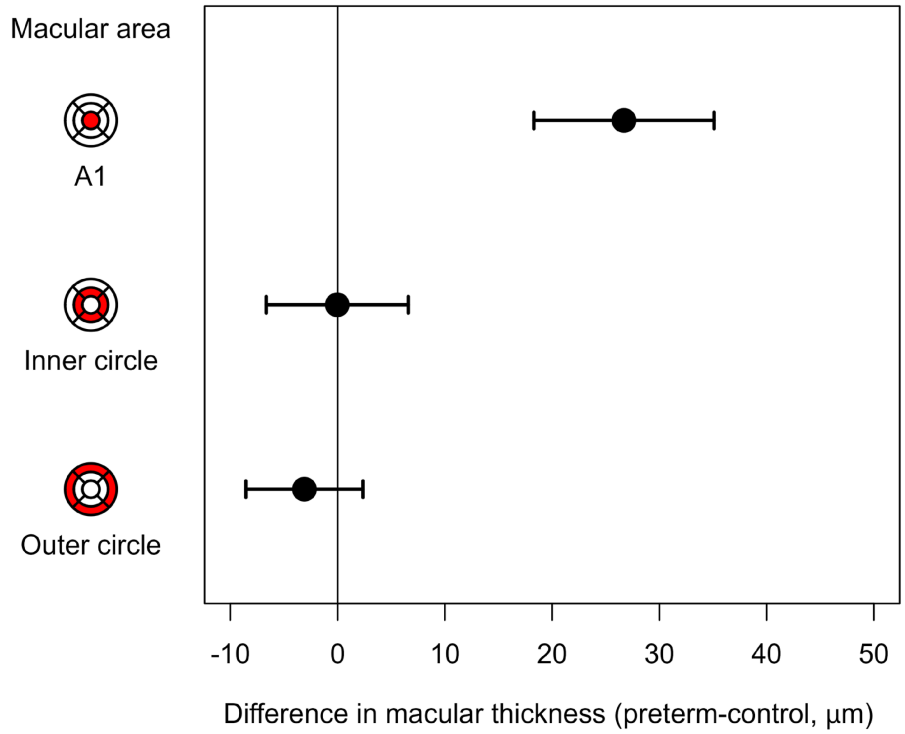

FIGURE 2 Difference (µm) in macular thickness between prematurely born individuals and controls.

Many OCT studies have reported on the macular retinal thickness and RNFL thickness in prematurely born children (Akerblom et al., 2011, 2012; Molnar et al., 2017), however, there are few studies performed in adults (Balasubramanian et al., 2019; Fieß, Pfisterer, et al., 2022; Nilsson et al., 2016). Nilsson et al. examined 14 ex-preterms, all treated with cryotherapy because of severe ROP, at an age of 24.5 years and found reduced foveal depth and altered distribution of RNFL in treated individuals compared to controls. Fieß et al. conducted a prospective study with 140 former preterm adults at the age of 18–51, born at a GA ≤32 weeks, of which 36 had previous ROP and seven had been treated, in a study on macular retinal and RNFL thickness. Balasubramanian et al. (2019) examined 133 extremely prematurely born individuals at 19 years of age and reported the central macular thickness.

The development of fovea and central macula has been evaluated in histological studies as well as in OCT studies. Maldonado and Toth (2013) used spectral domain OCT for analysing fovea in infants from postmenstrual age of 31 weeks up to adulthood. The authors found peripheral migration of the inner retinal layer and centripetal growth of the outer retinal layers in the first months of life. A progressive thinning of fovea and thickening of the parafoveal region with increasing age have been found (Maldonado & Toth, 2013; Vajzovic et al., 2012). In prematurely born children, a thicker macula has been found compared to full-term children, hypothesizing that the normal maturation of macula is disturbed by preterm birth (Venkataraman et al., 2023). Åkerblom et al. found that low GA was a risk factor for a thicker macula in preterm children; however, ROP was not. In contrast, Molnar et al. found that both GA and ROP were associated with increased macular thickness (Akerblom et al., 2011; Molnar et al., 2017). In the present cohort, we found that GA at birth remained correlated to a thicker macula also in adulthood, and that previous treatment of ROP was a risk factor for thicker macula in the multivariable analysis, in accordance with the study by Fieß, Pfisterer, et al. (2022). Nilsson et al. hypothesize that cryotherapy could be a factor leading to absence of foveal depression, thus a thicker macula (Nilsson et al., 2016). In the present study, we could not find any correlation between the best corrected VA and the thickness of central macula, in accordance with results from school-aged children (Akerblom et al., 2011; Molnar et al., 2017), albeit in contrast to Fieß, Pfisterer, et al. (2022). Likewise, there was no correlation with CS. The different results may be due to different cohorts in the studies.

The ganglion cell layer may be of interest in evaluating the optic nerve or visual pathway. It has been found to be reduced in optic nerve diseases and intracerebral lesions (Lee et al., 2018, 2019; Shinohara et al., 2022). As opposed to Balasubramanian et al., we found thinner GC-IPL in preterms than in full-term individuals and no impact regarding treated or untreated ROP (Balasubramanian et al., 2019). Similarly, GA or BW did not affect the GC-IPL in the preterms. Balasubramanian et al. found a weak correlation between decreased VA and thicker inner retinal layers (Balasubramanian et al., 2019), while we found no correlations between GC-IPL thickness and the best corrected VA or CS. The difference could be explained by different imaging techniques and software solutions.

Preterm birth affects the peripapillary RNFL thickness at school-age according to multiple previous studies (Akerblom et al., 2012; Fieß et al., 2017; Park & Oh, 2015; Ruberto et al., 2014). In accordance with Fieß et al., the average RNFL remained thinner in the prematurely

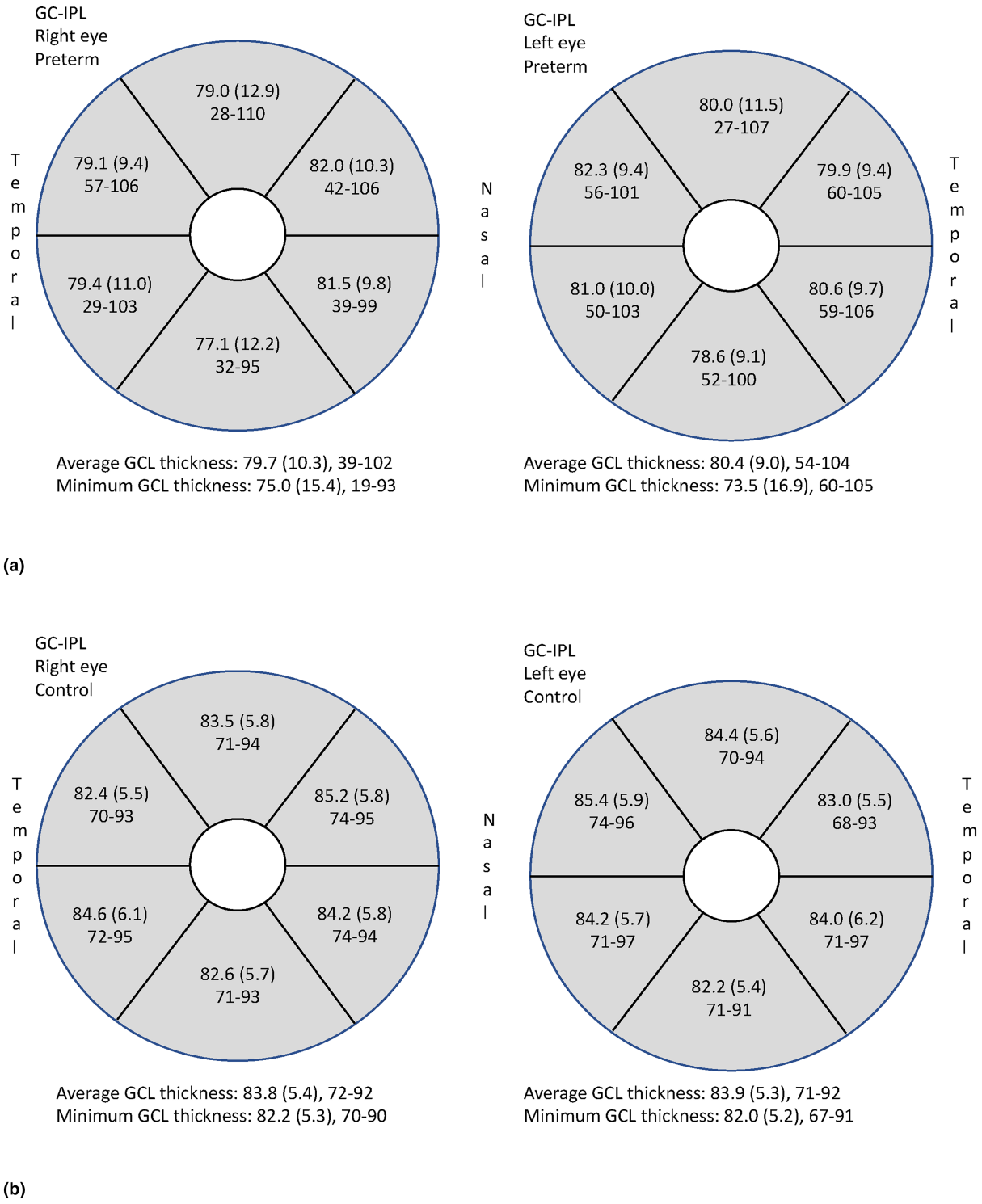

FIGURE 3 (a, b) Ganglion cell-inner plexiform layer (GC-IPL) thickness (μm), mean (standard deviation) and range. (a) Prematurely born individuals. (b) Controls.

born individuals compared to controls even into adulthood (Fieß, Schäffler, et al., 2022). However, in the study by Nilsson et al., no difference was found regarding average RNFL (Nilsson et al., 2016).

In the present study, the former prematurely born individuals who had been treated for severe ROP in the neonatal period had a thicker average RNFL compared to untreated prematurely born (Table 3). We believe that this difference was explained by the thicker temporal sector, similar to the findings presented by Nilsson et al. and Fieß et al. who found thicker RNFL in the temporal sector in adults formerly treated for ROP (Fieß, Schäffler, et al., 2022; Nilsson et al., 2016). Our results contradict previous studies in children treated for ROP, in which the average RNFL was thinner or similar to that of untreated children. (Akerblom et al., 2012; Fieß et al., 2017; Park & Oh, 2015). It is possible to hypothesize that there could be a change over time in the RNFL thickness from school age to adulthood in the treated individuals. A study of peripapillary RNFL in patients who underwent panretinal photocoagulation for proliferative diabetic retinopathy showed a reduction in average RNFL after 2 years (Kim

TABLE 2 Retinal nerve fibre layer (RNFL) thickness in prematurely born individuals and controls as well as mean difference between the groups.

	Prematures		Controls		Mean difference prematures versus controls			
	Right eye	Left eye	Right eye	Left eye	Difference	Lower limit	Upper limit	*p*-Value
Average thickness (μm)								
Mean (SD)	90.96 (10.62)	92.27 (11.42)	96.55 (10.11)	95.91 (9.82)	−4.61	−8.66	−0.55	0.028
Range	71 to 129	70 to 126	74 to 121	77 to 116				
Superior quadrant (μm)								
Mean (SD)	111.42 (17.61)	116.52 (15.84)	117.77 (15.02)	120.55 (15.26)	−4.80	−10.91	1.32	0.127
Range	82 to 185	83 to 165	89 to 161	88 to 158				
Inferior quadrant (μm)								
Mean (SD)	117.73 (16.06)	119.18 (16.10)	127.20 (16.17)	127.84 (14.18)	−8.29	−14.03	−2.55	0.006
Range	90 to 175	83 to 158	99 to 172	101 to 157				
Nasal quadrant (μm)								
Mean (SD)	68.84 (11.32)	68.16 (12.61)	77.55 (13.48)	75.57 (15.92)	−7.80	−12.27	−3.33	0.001
Range	42 to 91	44 to 104	50 to 118	32 to 112				
Temporal quadrant (μm)								
Mean (SD)	65.62 (23.66)	65.14 (27.75)	64.02 (6.96)	59.98 (7.02)	1.97	−6.36	10.31	0.643
Range	39 to 190	36 to 179	49 to 82	48 to 79				

Abbreviation: SD, standard deviation.

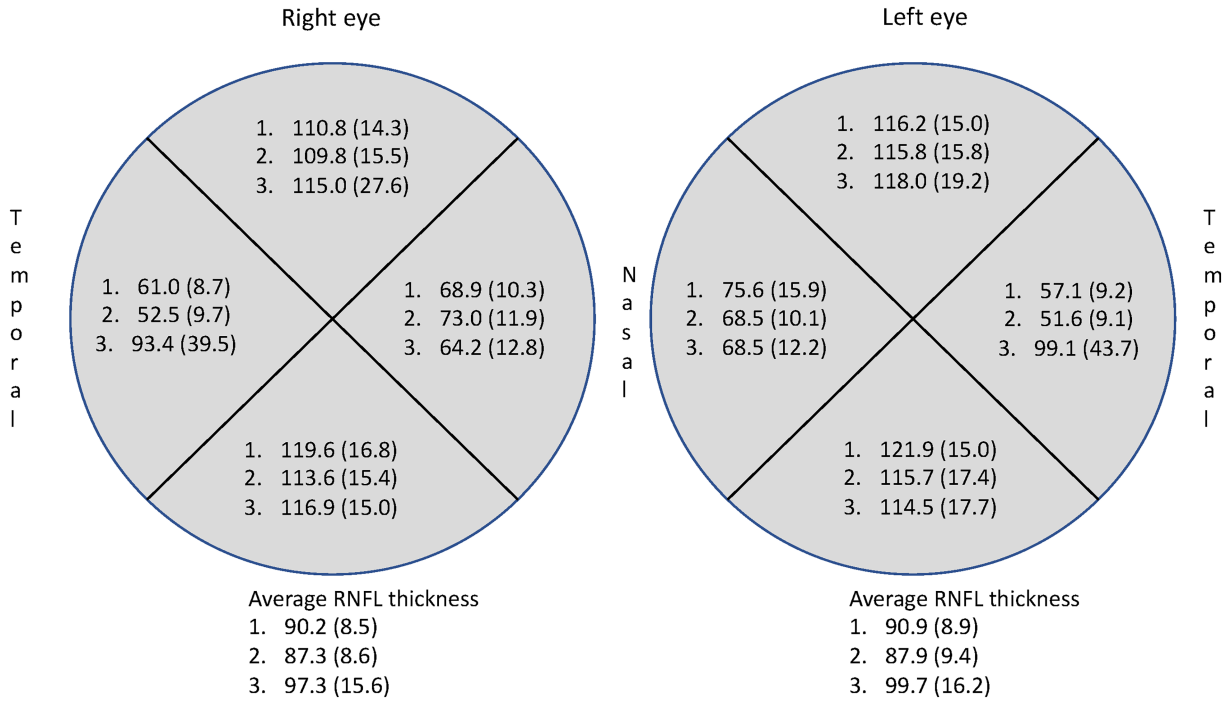

FIGURE 4 Retinal nerve fibre layer (RNFL) thickness (μm), in the preterm group according to 1: No ROP, 2: Untreated ROP and 3: Treated ROP. ROP, retinopathy of prematurity.

et al., 2012). However, the RNFL increased in the temporal sector; moreover, compared to control subjects, there was a significantly increased thickness, in line with the results from our study, in subjects formerly treated for ROP. One can only speculate whether the change comprises a compensatory regeneration in the nerve fibre layer around the optic nerve. Larger longitudinal studies over time in treated children might clarify this issue. Thicker peripapillary RNFL was correlated with worse logMAR VA and CS. A possible explanation is the effect of the temporal thickness seen in individuals formerly treated for ROP.

4.1 | Strengths and limitations

This study is one of few conducted with formerly prematurely born adult individuals, where ROP and its treatment in the neonatal period were known. Thus, it provides an insight into the long-term effects of preterm birth on retinal structure. The prematurely born individuals have been followed since birth, and a majority of the control group has been followed from 10 years of age.

One limitation was that no previous OCT had been performed in childhood, since the technique was not in

TABLE 3 Statistically significant risk factors regarding central macular thickness (A1) and average retinal nerve fibre layer (RNFL).

	Estimate	Confidence interval	*p*-Value
A1			
Gestational age (weeks)	−3.65	−6.37 to −0.94	0.011
Treated ROP	14.75	0.33 to 29.18	0.050
RNFL			
Treated ROP	9.09	2.54 to 15.64	0.009

Abbreviation: ROP, retinopathy of prematurity.

clinical use at that time. Longitudinal individual comparison could therefore not be performed. Further, the attendance rate of the original cohort was low.

5 | CONCLUSION

Central macular thickness was increased, and the macular ganglion cell layer was thinner in prematurely born young adults as compared to term born controls. Within the preterm group, we found that lower GA and treated ROP were risk factors for a thicker macula;

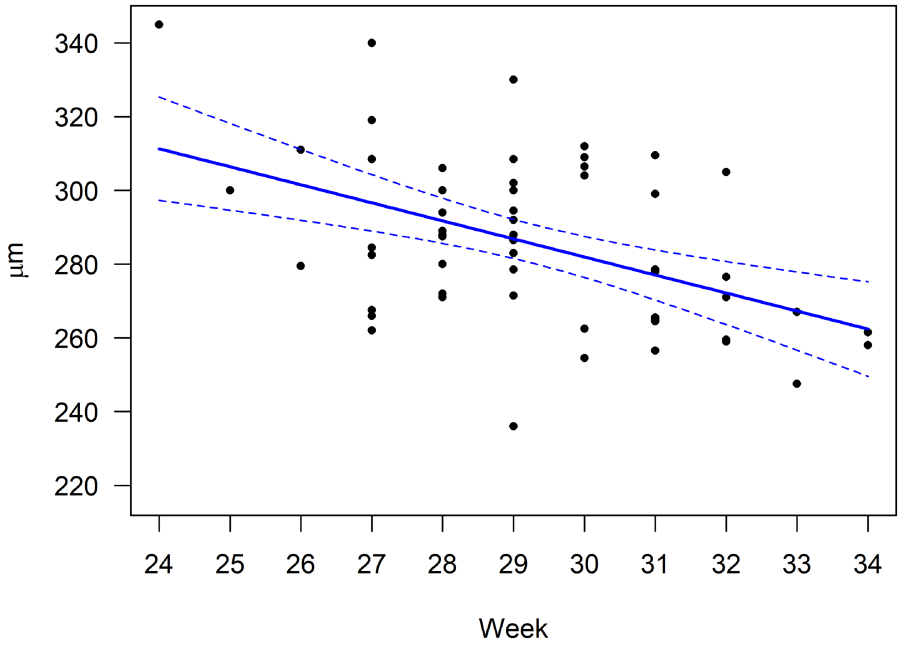

FIGURE 5 Scatter plot showing central macular thickness (A1, µm) in prematurely born individuals, born at different gestational ages.

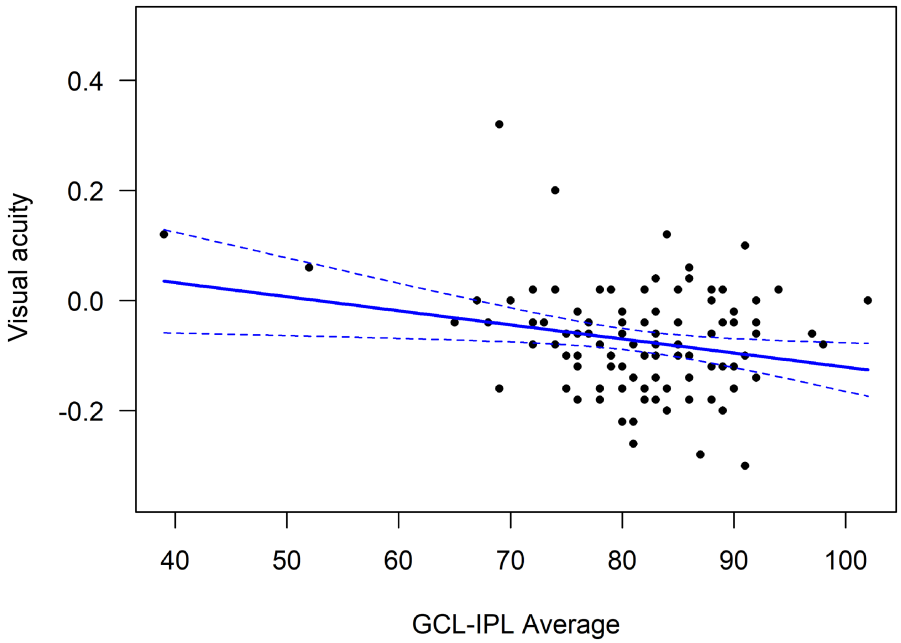

FIGURE 6 Scatter plot showing ganglion cell-inner plexiform layer (GC-IPL) thickness (µm) in prematurely born individuals with different visual acuities (logMAR).

however, we did not see the same risk factors for reduced GC-IPL. The prematurely born individuals had thinner average peripapillary RNFL than the controls. Within the group of prematurely born individuals, previous treatment for ROP was associated with thicker RNFL.

Further, within the group of prematurely born individuals, thicker average GC-IPL and thinner optic nerve RNFL were associated with better VA and CS.

ACKNOWLEDGEMENTS

We sincerely thank study nurse Eva Nuija, for her skilled work on the study, as well as Marcus Thuresson PhD, for assistance with the statistical analysis and for creating Figures 2, 5, and 6. The study received funding from Ögonfonden, The Carmen and Bertil Regnér Foundation, The Crown Princess Margaretha Foundation for the Visually Impaired and Synskadades Vänner i Uppsala län. The funders were not involved in the study design, nor the collection, analysis or interpretation of data, the writing of the report or in the decision to submit the manuscript for publication.

ORCID

Dýrleif Pétursdóttir https://orcid.org/0000-0002-9757-1373
Gerd Holmström https://orcid.org/0000-0002-5600-7186
Eva Larsson https://orcid.org/0000-0001-9674-0094

REFERENCES

Akerblom, H., Holmstrom, G., Eriksson, U. & Larsson, E. (2012) Retinal nerve fibre layer thickness in school-aged prematurely-born children compared to children born at term. *The British Journal of Ophthalmology*, 96, 956–960.

Akerblom, H., Larsson, E., Eriksson, U. & Holmstrom, G. (2011) Central macular thickness is correlated with gestational age at birth in prematurely born children. *The British Journal of Ophthalmology*, 95, 799–803.

Balasubramanian, S., Beckmann, J., Mehta, H., Sadda, S.R., Chanwimol, K., Nassisi, M. et al. (2019) Relationship between retinal thickness profiles and visual outcomes in young adults born extremely preterm: the EPICure@19 study. *Ophthalmology*, 126, 107–112.

de Kieviet, J.F., Zoetebier, L., van Elburg, R.M., Vermeulen, R.J. & Oosterlaan, J. (2012) Brain development of very preterm and very low-birthweight children in childhood and adolescence: a meta-analysis. *Developmental Medicine and Child Neurology*, 54, 313–323.

Early Treatment Diabetic Retinopathy Study Research Group. (1985) Photocoagulation for diabetic macular edema. Early treatment diabetic retinopathy study report number 1. *Archives of Ophthalmology*, 103, 1796–1806.

Express Group. (2010) Incidence of and risk factors for neonatal morbidity after active perinatal care: extremely preterm infants study in Sweden (EXPRESS). *Acta Paediatrica*, 99, 978–992.

Fieß, A., Janz, J., Schuster, A.K., Kölb-Keerl, R., Knuf, M., Kirchhof, B. et al. (2017) Macular morphology in former preterm and full-term infants aged 4 to 10 years. *Graefe's Archive for Clinical and Experimental Ophthalmology*, 255, 1433–1442.

Fieß, A., Pfisterer, A., Gißler, S., Korb, C., Mildenberger, E., Urschitz, M.S. et al. (2022) Retinal thickness and foveal hypoplasia in adults born preterm with and without retinopathy of prematurity: the Gutenberg prematurity eye study. *Retina*, 42, 1716–1728.

Fieß, A., Schäffler, A., Mildenberger, E., Urschitz, M.S., Wagner, F.M., Hoffmann, E.M. et al. (2022) Peripapillary retinal nerve fiber layer thickness in adults born extremely, very, and moderately preterm with and without retinopathy of prematurity: results from the Gutenberg prematurity eye study (GPES). *American Journal of Ophthalmology*, 244, 88–97.

Hellström, A., Smith, L.E. & Dammann, O. (2013) Retinopathy of prematurity. *Lancet*, 382, 1445–1457.

Hendrickson, A., Possin, D., Vajzovic, L. & Toth, C.A. (2012) Histologic development of the human fovea from midgestation to maturity. *American Journal of Ophthalmology*, 154, 767–778. e762.

Holmstrom, G., el Azazi, M., Jacobson, L. & Lennerstrand, G. (1993) A population based, prospective study of the development of ROP in prematurely born children in the Stockholm area of Sweden. *The British Journal of Ophthalmology*, 77, 417–423.

Holmstrom, G., el Azazi, M. & Kugelberg, U. (1999) Ophthalmological follow up of preterm infants: a population based, prospective study of visual acuity and strabismus. *The British Journal of Ophthalmology*, 83, 143–150.

Holmstrom, G. & Larsson, E. (2008) Long-term follow-up of visual functions in prematurely born children—a prospective population-based study up to 10 years of age. *Journal of AAPOS*, 12, 157–162.

Kim, J., Woo, S.J., Ahn, J., Park, K.H., Chung, H. & Park, K.H. (2012) Long-term temporal changes of peripapillary retinal nerve fiber layer thickness before and after panretinal photocoagulation in severe diabetic retinopathy. *Retina*, 32, 2052–2060.

Lee, J.Y., Ahn, J., Yoon, E.J., Oh, S., Kim, Y.K. & Jeon, B. (2019) Macular ganglion-cell-complex layer thinning and optic nerve integrity in drug-naïve Parkinson's disease. *Journal of Neural Transmission (Vienna)*, 126, 1695–1699.

Lee, J.Y., Choi, J.H., Park, K.A. & Oh, S.Y. (2018) Ganglion cell layer and inner plexiform layer as predictors of vision recovery in ethambutol-induced optic neuropathy: a longitudinal OCT analysis. *Investigative Ophthalmology & Visual Science*, 59, 2104–2109.

Maldonado, R.S. & Toth, C.A. (2013) Optical coherence tomography in retinopathy of prematurity: looking beyond the vessels. *Clinics in Perinatology*, 40, 271–296.

Molnar, A.E.C., Rosen, R.M., Nilsson, M., Larsson, E.K.B., Holmstrom, G.E. & Hellgren, K.M. (2017) Central macular thickness in 6.5-year-old children born extremely preterm is strongly associated with gestational age even when adjusted for risk factors. *Retina*, 37, 2281–2288.

Nilsson, M., Hellström, A. & Jacobson, L. (2016) Retinal sequelae in adults treated with cryotherapy for retinopathy of prematurity. *Investigative Ophthalmology & Visual Science*, 57, 550–555.

Park, K.A. & Oh, S.Y. (2015) Retinal nerve fiber layer thickness in prematurity is correlated with stage of retinopathy of prematurity. *Eye (London, England)*, 29, 1594–1602.

Pétursdóttir, D., Holmstrom, G. & Larsson, E. (2020) Visual function is reduced in young adults formerly born prematurely: a population-based study. *The British Journal of Ophthalmology*, 104, 541–546.

Pétursdóttir, D., Holmström, G. & Larsson, E. (2022a) Refraction and its development in young adults born prematurely and screened for retinopathy of prematurity. *Acta Ophthalmologica*, 100, 189–195.

Pétursdóttir, D., Holmström, G. & Larsson, E. (2022b) Strabismus, stereoacuity, accommodation and convergence in young adults born premature and screened for retinopathy of prematurity. *Acta Ophthalmologica*, 100, e791–e797.

Pétursdóttir, D., Holmstrom, G., Larsson, E. & Bohm, B. (2021) Visual-motor functions are affected in young adults who were born premature and screened for retinopathy of prematurity. *Acta Paediatrica*, 110, 127–133.

Provis, J.M., Diaz, C.M. & Dreher, B. (1998) Ontogeny of the primate fovea: a central issue in retinal development. *Progress in Neurobiology*, 54, 549–580.

Rothman, A.L., Sevilla, M.B., Mangalesh, S., Gustafson, K.E., Edwards, L., Cotten, C.M. et al. (2015) Thinner retinal nerve fiber layer in very preterm versus term infants and relationship to brain anatomy and neurodevelopment. *American Journal of Ophthalmology*, 160, 1296–1308.e1292.

Ruberto, G., Angeli, R., Tinelli, C., Bianchi, P.E. & Milano, G. (2014) Morphologic and functional analysis of the optic nerve in premature and term children with OCT, HRT, and pVEP: a 10-year

resurvey. *Investigative Ophthalmology & Visual Science*, 55, 2367–2375.
Saigal, S. & Doyle, L.W. (2008) An overview of mortality and sequelae of preterm birth from infancy to adulthood. *Lancet*, 371, 261–269.
Shinohara, Y., Todokoro, D., Yamaguchi, R., Tosaka, M., Yoshimoto, Y. & Akiyama, H. (2022) Retinal ganglion cell analysis in patients with sellar and suprasellar tumors with sagittal bending of the optic nerve. *Scientific Reports*, 12, 11092.
Vajzovic, L., Hendrickson, A.E., O'Connell, R.V., Clark, L.A., Tran-Viet, D., Possin, D. et al. (2012) Maturation of the human fovea: correlation of spectral-domain optical coherence tomography findings with histology. *American Journal of Ophthalmology*, 154, 779–789.e772.
Venkataraman, A.P., Popovic, Z., Hellgren, K., Sjöstrand, J. & Nilsson, M (2023) Structural impact of arrested foveal development in children born extremely preterm without ROP at 6.5 years of age. *Eye (Lond.)*, 37, 1810–1815.
Yanni, S.E., Wang, J., Chan, M., Carroll, J., Farsiu, S., Leffler, J.N. et al. (2012) Foveal avascular zone and foveal pit formation after preterm birth. *The British Journal of Ophthalmology*, 96, 961–966.

How to cite this article: Pétursdóttir, D., Åkerblom, H., Holmström, G. & Larsson, E. (2023) Central macular morphology and optic nerve fibre layer thickness in young adults born premature and screened for retinopathy of prematurity. *Acta Ophthalmologica*, 00, 1–10. Available from: https://doi.org/10.1111/aos.15814