Article

Distinguishing Familial from Acquired Traits in the Retinal Blood Vessel Arborization

Anne Bouthillier[1], Louis-Félix Berthiaume[1], Anne Xuan-Lan Nguyen[1], Shu Yi Zhai[1], Sarina Lalla[1], Olivier Bédard[1], Mathieu Gauvin[1], John M. Little[1,*], and Pierre Lachapelle[1]

[1] Department of Ophthalmology & Visual Sciences, Research Institute of the McGill University Health Centre–Montreal Children's Hospital, Montreal, QC, Canada

Purpose: It has been suggested that retinal blood vessel arborization (RBVA) is unique to each individual. We examined this claim in a pedigree that included two pairs of monozygotic twins.

Methods: Fundus photographs were taken of subjects belonging to this pedigree to compare the pattern of their RBVA. Pattern prevalence within the general population was estimated from a pre-existing clinical database.

Results: The optic nerve head (ONH) RBVA disclosed the following patterns: pattern A, outgrowth, with angle sizes ranging from 12° to 86°, toward the macula, made by the central retinal (CR) vein; pattern O, circular shape delimited by the CR artery on the nasal side and CR vein on the temporal (macula) side; and pattern Y, a double-Y shape (upright in the superior retina and upside down in the inferior retina) made by the four branches—inferior temporal and nasal and superior temporal and nasal—of the CR artery. The prevalence of patterns A, O, and Y was estimated at 11%, 2.8%, and 2.7%, respectively, from our pre-existing clinical database. Pattern A was the most frequently noted in our pedigree, with a prevalence of 26% to 29%, a value significantly larger ($P < 0.05$) than that measured in our sample of the general population. Of note, familial similarity is progressively lost as we move away from the ONH.

Conclusions: Relatives appear to share similar ONH RBVA patterns, suggesting that the ONH RBVA could be genetically transmitted as a familial trait. Arrangement of the more peripheral retinal blood vessels would create individuality.

Translational Relevance: Our results suggest the existence of a specific, reproducible, and transmissible retinal identifier, a feature that could potentially be associated with the prevalence of a given disease process, thus offering the possibility of identifying an underlying retinopathy long before its clinical manifestation and consequently optimize its management.

Introduction

Modern technologies, such as security systems or personal recognition devices, sometimes make use of retinal scans to identify individuals.[1] To do so, digital images of the retinal fundus are processed using computerized algorithms that extract and quantify the features of the retinal vasculature, such as the angle of the vessels, number of vessels, density of the distribution, distance between vessels and the optic disc, vessel endings, bifurcations, and sizes, to name a few.[2] The rationale for the use of this biometric identification technique is that the pattern for retinal blood vessel arborization (RBVA)—the overall organization of the retinal arterial and venous vasculatures from the optic nerve head (ONH) to the retinal periphery (ora serrata)—is claimed to be distinct for each individual, even between monozygotic twins.[3,4] It is as if the RBVA was randomly assigned to a given individual with no input from our genetic background, including inheritance; however, in his study, Tower[4]
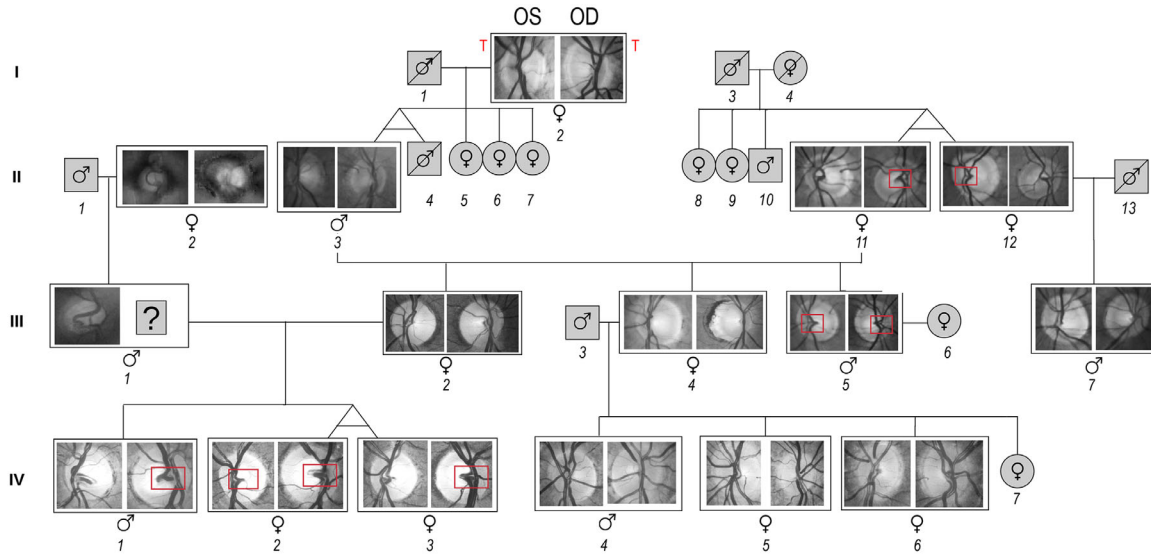
Figure 1. Four-generation (I–IV) pedigree showing transmission of the pattern A ONH RBVA (framed in *red* in optic discs of individuals of the family presenting it). Only subjects available for fundus photography are shown. The Canon CR-DGI Non-Mydriatic Retinal Camera was used for all fundus photography, except for subjects II-2 and III-1, who were photographed with the D-EYE digital fundus camera for practical reasons. Eye orientation is shown with fundi of subject I-2, where T indicates temporal (macula) side.

noted that, although the entire RBVA of monozygotic twins differed substantially, the arrangement of the blood vessels (arteries and veins) at and around the ONH shared some similarities. Could this observation suggest the possibility that some aspects of the RBVA are genetically determined and thus inherited?

Given that several aspects of our makeup are genetically determined (several of which are intimately shared between monozygotic twins), the fact that the RBVA would be left to chance is mystifying, more so when one considers the scarcity of studies supporting this dogma. Unfortunately, to this date, there is no evidence suggesting that the RBVA is an inheritable (transmissible) trait, although some studies did report that some features of it, such as tortuosity,[5] blood vessel diameter,[5] or presence/absence of cilioretinal arteries[6], appeared to follow a pattern of inheritance. Along the same lines of evidence, several features of the ONH itself, such as disc size, cup size, and cup-to-disc ratio, have been shown to be inheritable,[7,8] suggesting that the retina can disclose inheritable traits, provided we carefully look for them. Along those lines, a recent cross-sectional study compared the retinal vasculature of twins and showed that the branching pattern of the retinal vascular tree (i.e., the fractal dimension) was more similar in monozygotic compared to dizygotic twins.[9] The latter study also suggested that heredity accounted for 54% of the variation in the branching pattern of the RBVA, whereas 46% was individually (or environmentally) determined. Given that heredity appears to play a key role in the design of the retinal

vascular tree of monozygotic twins as suggested above, could this observation be extended to members of the same pedigree? In other words, could the RBVA also show more similarities between family members compared to a random sample of unrelated individuals? The purpose of this study was therefore to further investigate whether or not the RBVA does bear inheritable traits visible among members of the same family.

Methods

This study was conducted as part of an investigation, approved by the institutional review board of the McGill University Health Centre, on the maturation of retinal function (from infants to adulthood), a project that included multifocal electroretinography and imaging of the retinal fundus. The research followed the tenets of the Declaration of Helsinki. Informed consent was obtained from the subjects after receiving an explanation of the nature of the study. In the present study, only the results pertaining to the retinal fundus images are reported.

Retinal photographs were taken from 16 normal subjects (10 females and six males; age range, 4–94 years), all members of the four-generation pedigree of one of the co-authors (PL; subject II-3), as shown in Figure 1. The fundus camera used was the Canon CR-DGI Non-Mydriatic Retinal Camera (Canon, Inc., Tokyo, Japan). The visual angle of the
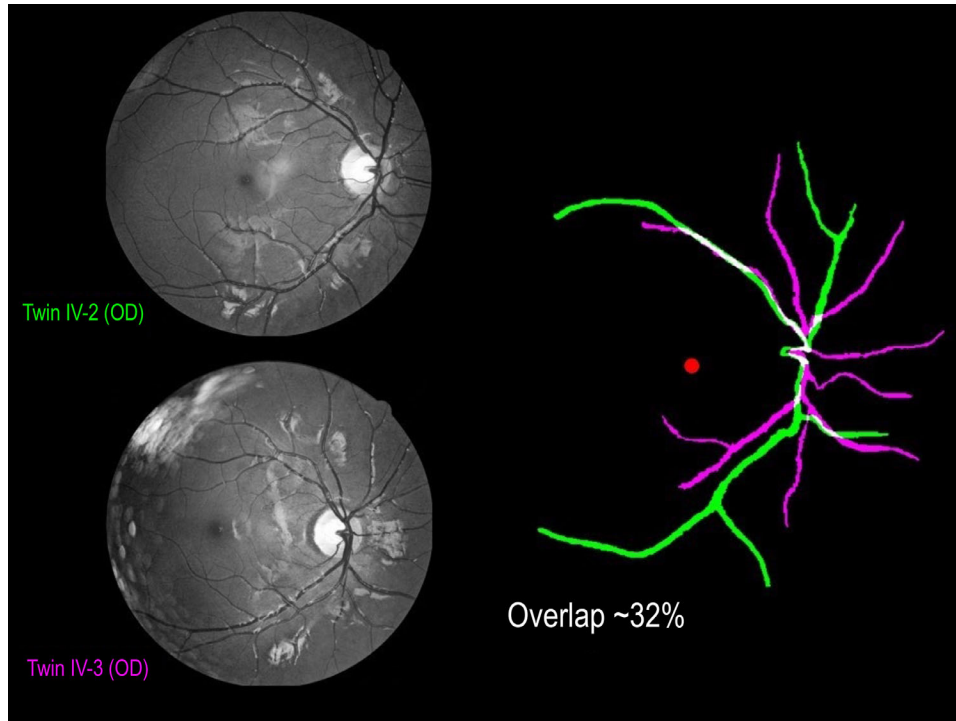
Figure 2. Fundus pictures of the right eyes of twins IV-2 and IV-3 with accompanying segmentation of the venous RBVA and corresponding overlap percentage (IV-2 in *green* and IV-3 in *magenta*). The *red dot* indicates the approximate position of the macula.

photographs is 45° and the resolution is 8 pixels. Note that fundus photographs of subjects II-2 and III-1 were taken with a D-EYE digital fundus camera (Padova, Italy) for practical reasons. This pedigree also included two sets of female monozygotic twins aged 67 years (subjects II-11 and II-12) and 12 years (subjects IV-2 and IV-3) at the time of fundus imaging. Of note, subject II-11 was also the grandmother to subjects IV-2 and IV-3.

Similarities between each member of the two monozygotic pairs of twins were evaluated by comparison of the RBVA of the left and right ONH. We first identified the ONH RBVA patterns A and O using a macroscopic (i.e., naked eye) analysis of fundus pictures of the two sets of twins. Given that the two pairs of twins were blood related, we then searched the pedigree to see if more individuals had A or O patterns. Only pattern A seemed to be reproduced in other individuals; however, the search revealed another pattern (Y) that also seemed to be shared by several individuals. Schematic drawings of these patterns were then made (for an example, see Fig. 10). Finally, in order to determine the population prevalence of the RBVA patterns noted within our pedigree, these schematic drawings were used to scan our database of 1698 eye fundus photographs (Kowa RC-2 handheld fundus camera; Kowa Company, Ltd., Aichi, Japan)

to look for similar patterns. From this exploration, we identified 197, 55, and 56 fundus pictures resembling patterns A, O, and Y, respectively. These findings were then verified (by AB) for validation, and 186 (94%), 49 (88%), and 46 (84%) of the pictures showing A, O, and Y patterns, respectively, were ultimately retained. Of note, from the 1698 fundus pictures that composed our database, only 281 (17%) were ultimately selected as belonging to patterns A, O, and Y, suggesting the existence of other types of ONH RBVA patterns that are not accounted for herein. This observation is also supported with the ONH RBVA of subjects that resisted our macroscopic classification (subjects I-2, II-2, II-3, III-1, and III-7).

Results

As a first attempt, the retinal fundus of the first set of twins was segmented to extract the retinal blood vessels (Fig. 2, subjects IV-2 and IV-3; only OD is shown). The veins of the RBVA of twin IV-2 were then colored in green and those of twin IV-3 in magenta, so that each time a pixel belonging to twin IV-2 overlapped one of twin IV-3, this would result in a white pixel. The number of white pixels was then
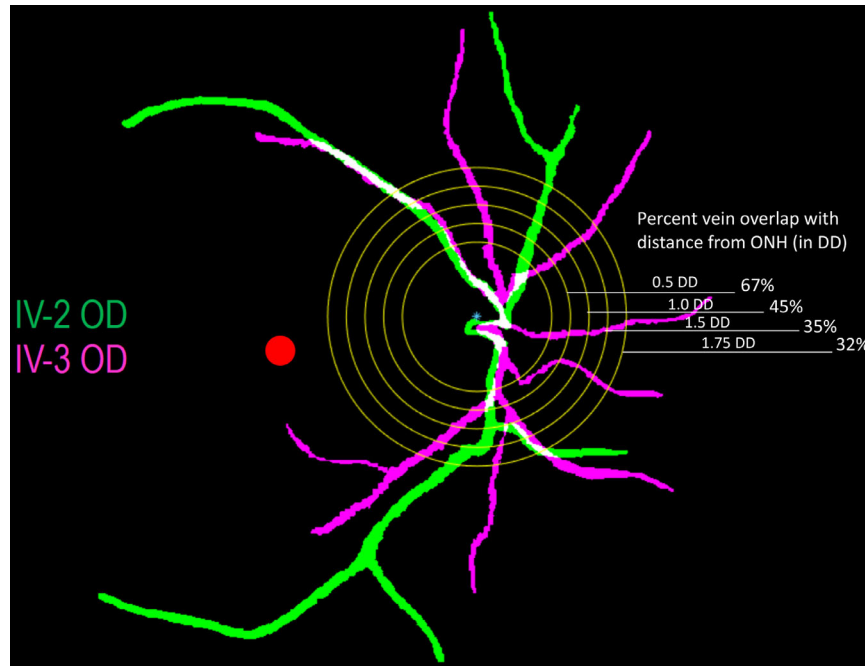
Figure 3. Superimposed RBVAs (veins only) of the right fundi of twins IV-2 (in *green*) and IV-3 (in *magenta*). Superimposed blood vessels yield white pixels (see text). Concentric circles represent distances of 1.0, 1.25, 1.50, and 1.75 DD from the ONH center. The percentages of vein overlap within each of these areas are noted. The *red dot* indicates the approximate position of the macula.

divided by the smallest number of colored pixels (green or magenta) to yield the percentage of overlap between the RBVA of both twins. This approach yielded a mere 32% overlap, indicating limited blood vessel superposition, as illustrated at the right-hand side of Figure 2.

While segmenting the RBVA, however, we noticed that the overlap became more prominent when only the blood vessels contained within the ONH were considered, a finding also reported in the study of Tower.[4] In order to confirm what we saw macroscopically with our method of superposition, we analyzed the RBVA
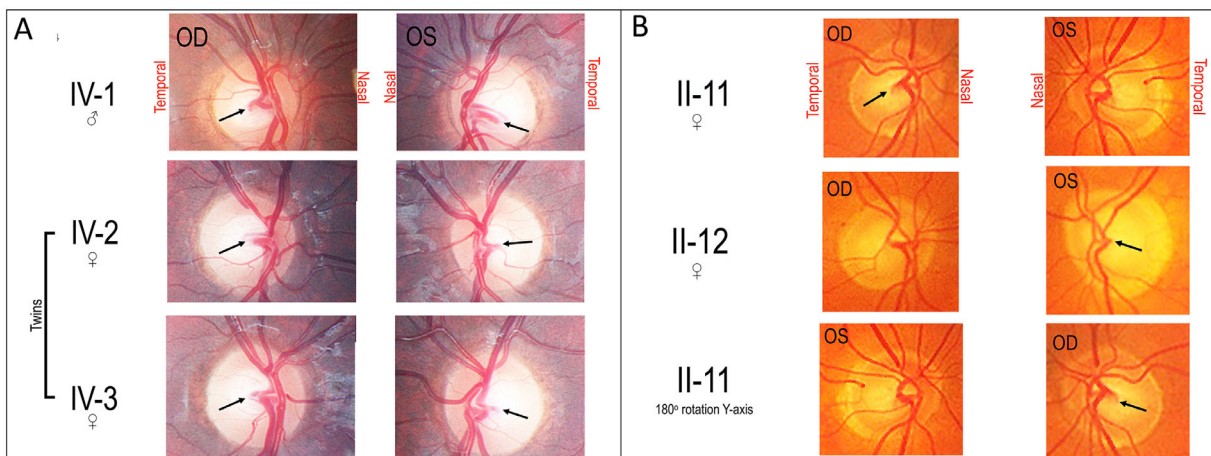

Figure 4. (A) Magnified ONH of the OD and OS fundi of subjects IV-1, IV-2, and IV-3 to enhance the pattern A features. The arrows point at the tip of outgrowth made by the central retinal vein (less obvious in the OS of subject IV-3). The T indicates the temporal (macula) side. (B) Magnified ONH of the OD and OS fundi of subjects II-11 and II-12 to enhance the features of patterns A and O. The arrows point at the tip of outgrowth made by the central retinal vein in the OD of subject II-11 and OS of subject II-12. Given the mirror-image presentation (i.e., the OD of subject II-11 is similar to the OS of subject II-12 and the OS of subject II-11 is similar to the OD of subject II-12), the fundus pictures of subject II-11 were rotated by 180° along the y-axis to allow comparison with subject II-12 (bottom pictures). The T indicates the temporal (macula) side.
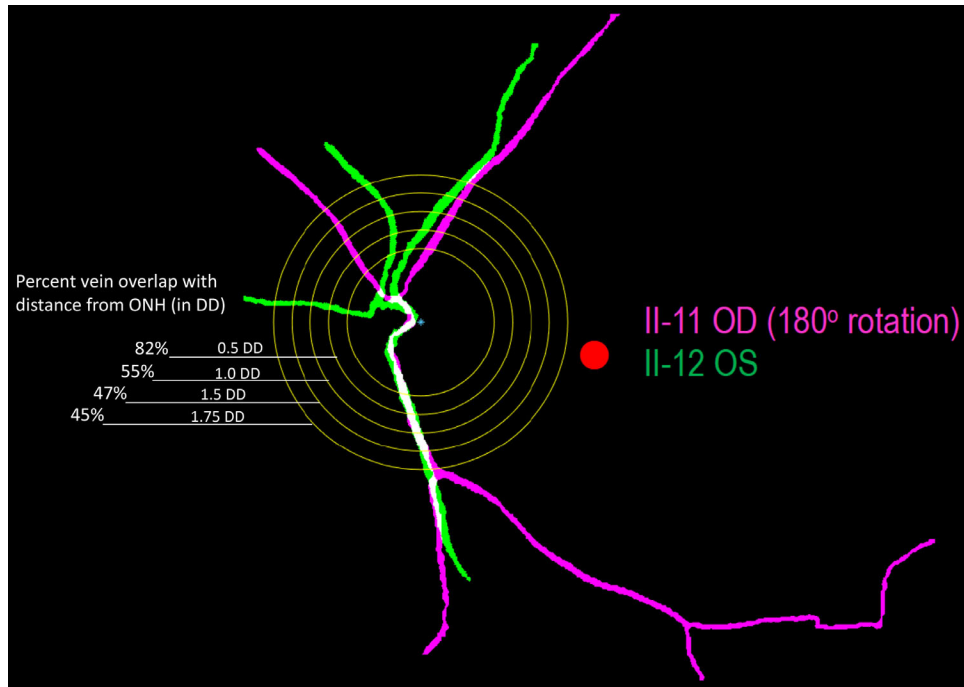
Figure 5. Superimposed RBVA of the right fundus of twin II-11 (180° rotation around the *y*-axis; in *magenta*) and of the left fundus of twin II-12 (in *green*). Superimposed blood vessels yield white pixels (see text). Concentric circles represent distances of 1.0, 1.25, 1.50, 1.75, and 1.75 DD from the ONH center. Percentages of vein overlap within each of these areas are noted. In twins IV-2 and IV-3, note the near perfect overlap of the superior temporal vein over more than 1.75 DD. The *red dot* indicates the approximate position of the macula.

superposition separately at different distances of the ONH. Figure 3 shows the superimposed RBVA (veins only) of the right eyes of twins IV-2 (in green) and IV-3 (in magenta). The RBVA values are shown with concentric circles with disc diameters (DD) of 0.5 to 1.75. The RBVA overlap decreases gradually as we move away from the center of the ONH, thus confirming the initial observation made by Tower in 1955.[4]

As can be seen in Figure 4A, both twins showed an outgrowth (identified with a black arrowhead) of the central retinal vein pointing toward the macula (pattern A), suggesting that twins could indeed share common RBVA features. Of note, the same pattern A was also identified in both eyes of their brother (Fig. 4A, subject IV-1). The same pattern was also noticed in the other set of twins belonging to this pedigree (subjects II-11 and II-12) (Fig. 4B). In the latter case, however, pattern A was present in only one eye (OD for twin II-11 and OS for twin II-12), whereas in the fellow eyes an O-shaped pattern—a circular space delimited by the central retinal vein temporally (i.e., towards the macula) and by the central retinal artery nasally, subsequently identified as pattern O—was observed in both twins, resulting in a mirror image effect. In other words, the OD of twin II-11 looks like the OS of twin II-12,

and the OS of twin II-11 looks like the OD of twin II-12). Of note, a similar mirror image presentation was also alluded to in Tower's study.[4] Figure 5 shows the superimposed RBVA (veins only) of the right eye (180° rotation in magenta) of twin II-11 and the left eye (in green) of twin II-12, the latter shown with concentric circles of 0.5 to 1.75 DD. As seen in the previous set of twins, the RBVA overlap decreased gradually as moving away from the center of the ONH.

Given that the same pattern A was observed in five different individuals (as reported above) belonging to the same pedigree, we wondered if more members of this pedigree shared this feature. Fundus inspection of the other members of this pedigree also revealed a well-defined pattern A in both eyes of subject III-4 (son of II-11 and uncle of IV-1, IV-2, and IV-3) and a subtler pattern A in both fundi of subject III-2 (the mother of twins IV-2 and IV-3); both sets of fundus pictures are shown in Figure 6. Thus, a clear pattern A was observed in generation II (subjects II-11 and II-12), generation III (subject III-5 and possibly subject III-2), and generation IV (subjects IV-1, IV-2, and IV-3), representing 26% to 29% of the fundi examined in this pedigree (eight or nine out of 31). Furthermore, when only considering the progeny of subject II-11,
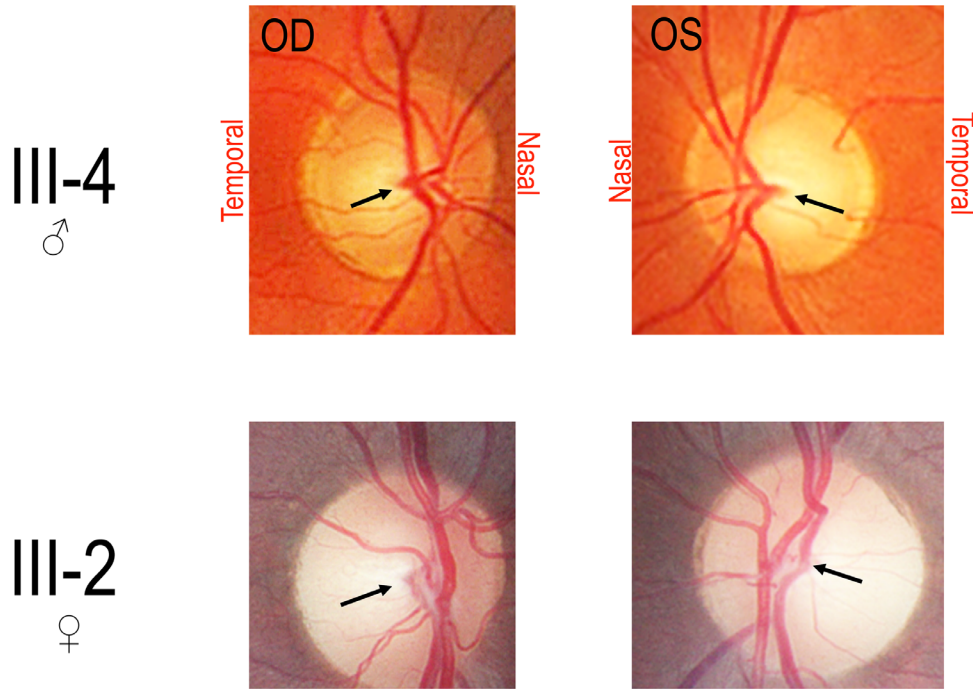
Figure 6. Magnified ONH of the OD and OS fundi of subjects III-2 and III-4 to enhance the features of pattern A. The arrows point at the tip of outgrowth made by the central retinal vein (less obvious for subject III-2). The T indicates the temporal (macula) side.
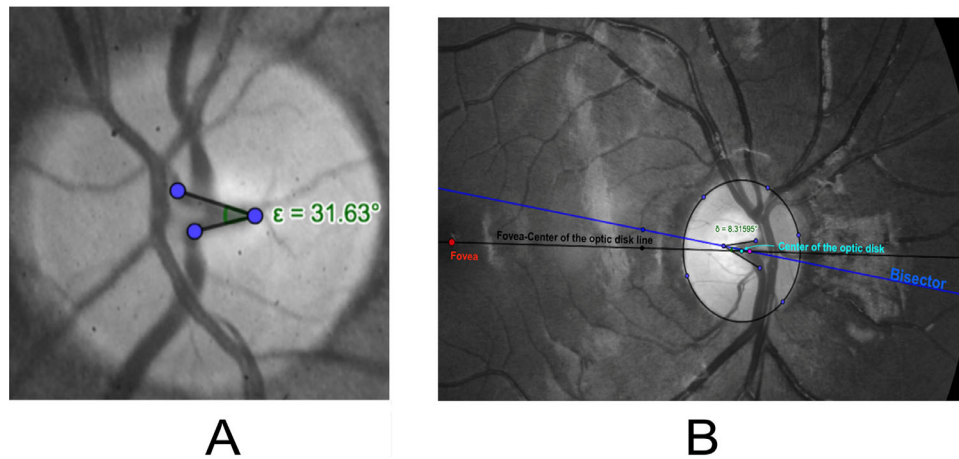

Figure 7. (A) The angle size of pattern A was measured as the angle formed by the two arms of the central retinal vein outgrowth toward the macula. (B) The direction in which pattern A outgrowth was measured as the angle formed between a straight line joining the ONH and macula (fovea) centers and the bisector of pattern A angle. Both measures were obtained using Geogebra freeware.

close to half of her descendants—four (or five if we include III-2) out of nine descendants (one or two out of three children and three out of seven grandchildren) examined—showed a pattern A RBVA in at least one eye. We now wonder if pattern A observed in this pedigree is also a feature common to most individuals. Fortunately, we had at our disposition a databank (gathered by JML and PL over ~40 years) of 1698 fundus pictures that we used to estimate the prevalence of pattern A. We found that pattern A was observed in only 11% of our sample population, a value far below the 26% to 29% of prevalence of pattern A in our pedigree ($P < 0.05$).

In order to further characterize pattern A, we measured the size of the angle made by the outgrowth of the central retinal vein, as well as the angle of

Table. Size and Direction of Pattern A Angles

Subject	Eye	Angle Size (°)	Direction (°)
II-11	OD	45.7	1.52
II-12	OS	33.3	9.24
III-2	OD	90.7	−3.75
III-5	OD	71.75	18.5
III-5	OS	40.1	21.3
IV-1	OD	39.4	7.1
IV-2	OD	38.3	9.18
IV-2	OS	36.3	21.5
IV-3	OD	44.8	8.32
Mean ± CV within pedigree	—	48.9 ± 19.3	10.3 ± 8.7
CV%	—	39	85
Mean ± CV within population	—	49 ± 19	1.98 ± 13
CV%	—	39	657
Confidence interval within population	—	12 to 86	−22.6 to +26.6

Angle size and direction for pattern A (as per Fig. 6). Out of the 1698 total fundi, 186 fundus photographs showed pattern A. CV, coefficient of variation.

direction to which it is pointing (Fig. 7). Results of these measurements (Table) revealed that the angle size measured within our pedigree was not significantly different ($P > 0.05$) from that measured within our normal population sample, each showing the same coefficient of variation. The angle and coefficient of variability measured within our two sets of twins were much smaller: 39.5° ± 8.8° with 22% variation for twins II-11 (OD) and II-12 (OS), and 39.8° ± 4.4° with 11% variation for twins IV-2 (OD + OS) and IV-3 (OD). The latter finding contrasts with the significantly larger ($P < 0.05$) variation measured for the angle of direction and does not allow us to distinguish our pedigree (even in the case of the twins) from our sample of the general population (Table).

Another transmitted ONH RBVA pattern could also be documented within our pedigree. This pattern (referred to as pattern Y) is formed of an upright and upside-down Y shape made by the superior (upright Y) and inferior (upside down Y) nasal and temporal branches of the central retinal artery (Fig. 8). This pattern, which was observed in 2.7% of our sample population, was seen in subject III-4 (the daughter of subject II-11) and in two of her children (subjects IV-6 and IV-4) but not in subject IV-5, whose intermediate segment was found to be too short to qualify for this pattern (i.e., closer to a X shape rather than a double upright and upside-down Y shape). Unfortunately, given the limited number of subjects available in generations I and II, we were not able to identify from whom subject III-4 inherited her ONH RBVA pattern Y. Finally, the ONH RBVA patterns of the remaining members of our pedigree (subjects I-2, II-2, II-3, III-1, and III-7) were not further analyzed given that they appeared to be singletons.

Discussion

The purpose of this study was to investigate if the RBVA was genetically determined and possibly an inheritable trait, a hypothesis that stemmed from a previous observation made by Tower[4] in his 1955 study of the RBVA in monozygotic twins. In this study, Tower[4] reported that when one considers the entire retinal vascular tree, monozygotic twins had little in common; however, when restricting the comparisons to the blood vessels contained within the ONH, identical twins did appear to share similar RBVA. This observation suggests that some aspects of the RBVA are genetically determined and possibly inherited (central RBVA), whereas others appear to be acquired (peripheral RBVA). This concept is best illustrated in Figures 3 and 5. In our two sets of twins, the RBVA overlap decreased gradually as we moved away from the center of the ONH, thus confirming the initial observation made by Tower.[4] It is worth mentioning, however, the near perfect overlap over more than 1.75 DD of the superior temporal vein (IV-2 vs. IV-3; Fig. 3) or inferior temporal vein (II-11 vs. II-12; Fig. 5), suggesting that the high similarity of some features of the RBVA in monozygotic twins might possibly extend beyond the ONH.
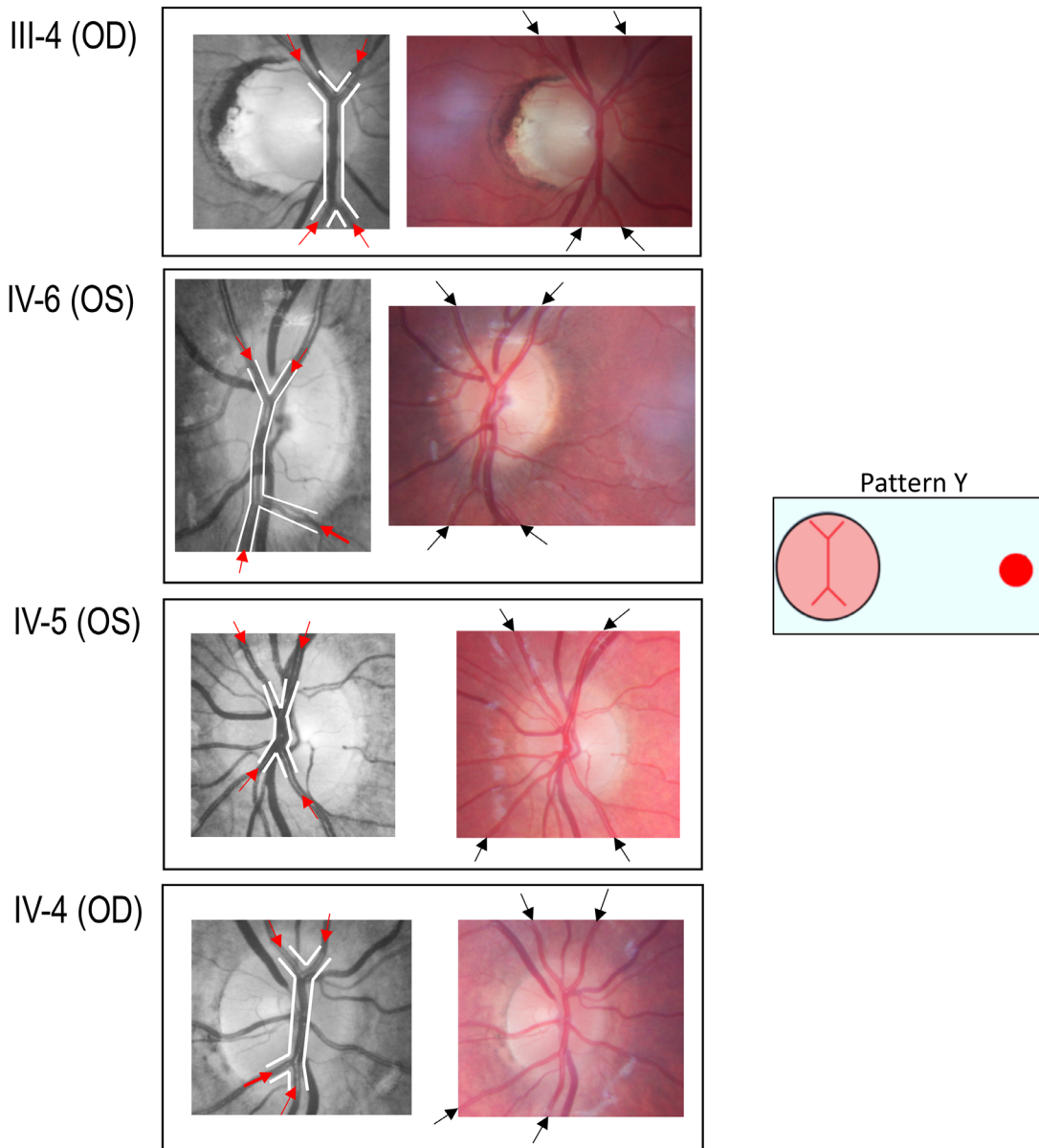
Figure 8. Magnified ONH of the OD and OS fundi of the mother (subject III-4) and three of her four children (subjects IV-4, IV-5, and IV-6) to enhance the features of pattern Y. The arrows point at the tip of the superior and inferior nasal and temporal retinal arteries (courses of which are shown in the black-and-white pictures) at the origin of this pattern, whose features are graphically represented at the center of the picture (ONH at left and macula at right). Pattern Y is clearly visible in the OD of subject IV-4 and in the OS of subject IV-6 but not in the OS of subject IV-5 due to a too-short middle segment (more like a X shape).

This result, combined with our demonstration of a familial transmission of ONH RBVA pattern, suggests that the latter would have a stronger genetic contribution when compared to the peripheral RBVA. Of note, a study on the vascularization of the human fetal retina showed that, although vasculogenesis was at the origin of the primitive vessels of the central inner retina (at the ONH level), angiogenesis governed their extension toward the periphery of the retina.[10] This study also revealed that the angiogenesis phase appeared to be triggered and maintained by the hypoxia-induced vascular endothelial growth factor, but the vasculogenesis phase was not. It follows that different genes are most probably responsible for these two particular embryological processes and could account for the difference in RBVA heritability moving away from the ONH. This distinction was also documented in a previously reported patient of ours affected with retinitis pigmentosa that we followed for close to three decades.[11] Figure 9 shows the superposition of the
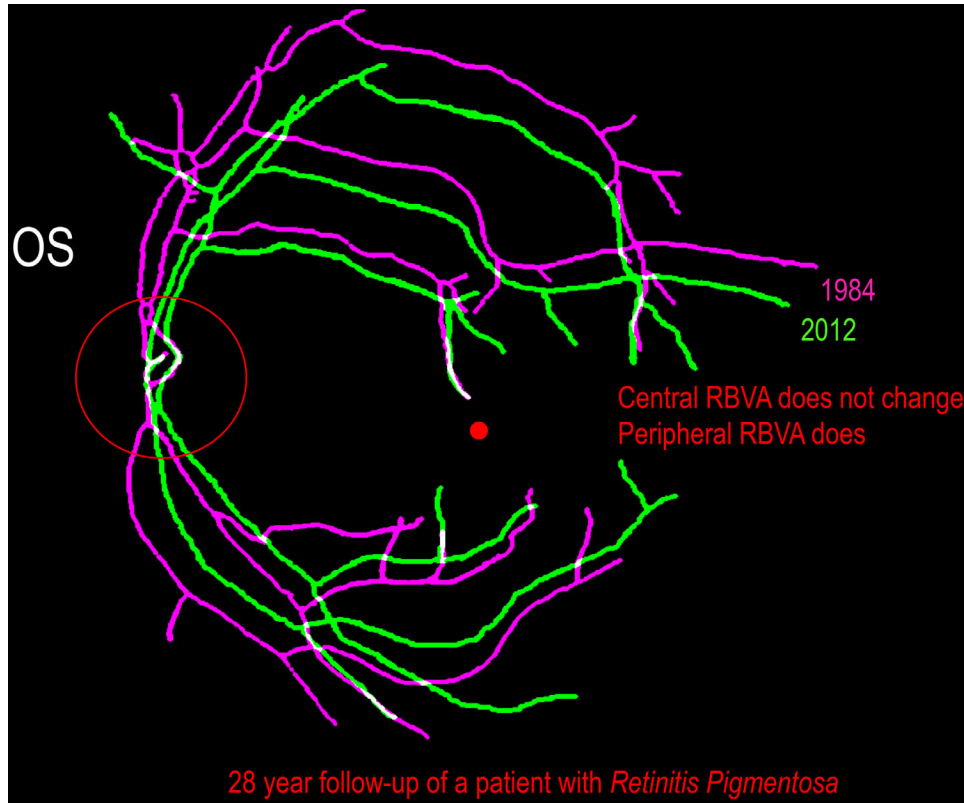
Figure 9. The superimposed RBVA (arteries and veins) of a patient affected with retinitis pigmentosa. Fundus pictures were obtained in 1984 (*magenta*) and in 2012 (*green*) with the same camera and by the same individual (JML). Of note, white pixels are primarily seen at the center of the ONH where the RBVA forms a pattern D shape. The *red dot* indicates the approximate position of the macula.

RBVA obtained at two visits (1984, magenta; 2012, green) 28 years apart. The ONH RBVA pattern of that patient presented as a D shape (pattern D, seen in 1.9% of our sample of the general population) made by an outgrowth of the central retinal artery pointing toward the macula, which is surrounded by a loop made by the central vein. This pattern remained identical throughout the 28 years of follow-up, as exemplified by the large number of white pixels indicative of perfect superposition. The latter contrasts with the near absence of superposed vessels outside of the ONH center, presumably the result of displacement of the peripheral retinal vessels secondary to the retinitis pigmentosa disease process.

As shown in Figure 10, the four different ONH RBVA patterns that we have identified to date have respective prevalence values ranging from 1.9% for pattern D to 11% for pattern A, the first pattern that we observed (thus explaining its identification as pattern A). Although it is too early to predict how many RBVA possibilities may exist, it is worth mentioning that a recent publication included fundus pictures (OD and OS) in which the ONH RBVA was similar to that of subjects II-11 and II-12 in our pedigree.[12] In this study, pattern O was seen in OD and pattern A in OS, a presentation identical to that of our subject II-12 (Fig. 4B). These results would support not only a finite amount of ONH RBVA but also a finite number of OD and OS ONH RBVA combination possibilities.

It is worth re-emphasizing that the findings reported herein were based on observations made on a single, albeit relatively large, pedigree. Some could see this as a limitation or weakness, thus requiring validation of our conclusions with a larger sample. Although we do not dispute this claim, we believe that it is important to take into consideration the following key elements in support of our demonstration: We were able to identify, within our pedigree, two different ONH RBVA that were transmitted over two (pattern Y) or three (pattern A) generations. These patterns were also shown to be present in the normal population with prevalence rates of 2.7% (pattern Y) and 11% (pattern A), respectively. In addition, the unusual combination of pattern A and pattern O observed in twins ll-11 and ll-12 was also seen elsewhere.[12] To us, these findings suggest that these ONH RBVA patterns are not fortuitous observations; rather, they are real, genetically determined, and transmissible as a familial trait. Another
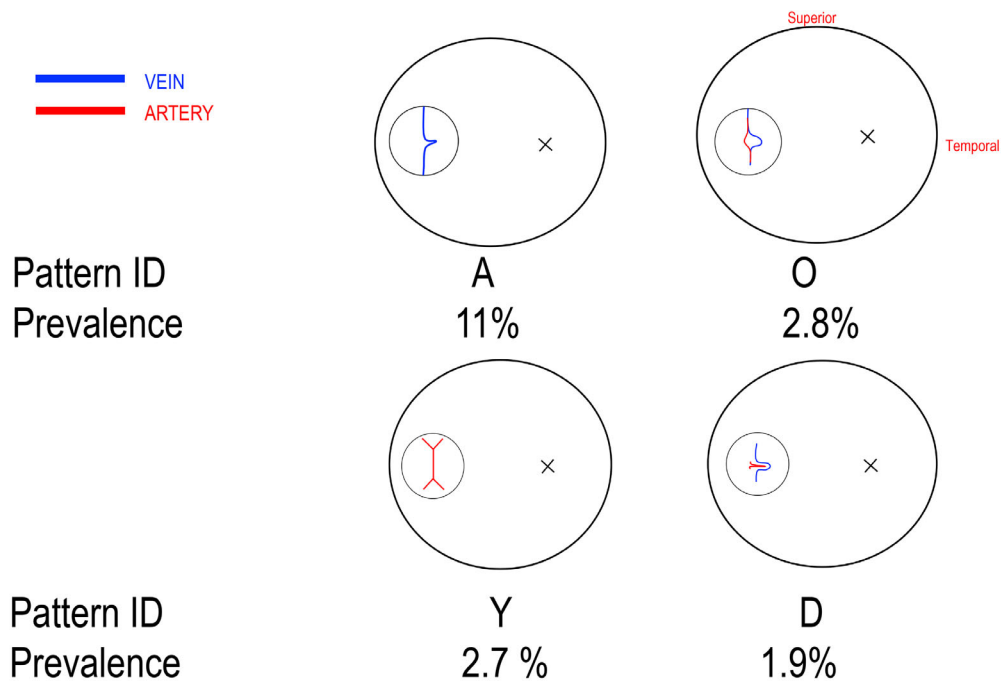
Figure 10. Left eye schematic representations of the different ONH RBVA patterns (identified with corresponding letters at the bottom of each RBVA pattern) found to date, along with respective prevalence values measured in a database of 1698 fundus photographs. Central retinal arteries and veins are represented with *red* and *blue lines*, respectively. The macula is identified with an X. Note that patterns A, O, Y, and D were binocular 60%, 24%, 13%, and 57% of the time, respectively.

limitation is the possibility that the specific patterns of the ONH RBVA could be altered or modified by a given disease process known to affect the retinal vasculature at the ONH, such as glaucoma, hypertension, cerebrospinal fluid pressure, or even hematocrit level.[13,14] Although the impact of this possible limitation will have to be evaluated, we do not believe that it will change the essence of our report, which is that the ONH RBVA is genetically determined and transmissible as a familial trait.

In conclusion, our results demonstrate that some features of the RBVA at the level of the ONH are not only genetically determined but also transmitted as a familial trait from one generation to the next—three generations for pattern A and two for pattern Y. To our knowledge, this is the first demonstration suggesting that the arrangement of the retinal blood supply has a genetic incidence and is also transmissible as a familial trait. The existence of a specific, reproducible, and transmissible retinal identifier could potentially be associated with the prevalence of a given disease process, thus offering the possibility of identifying an underlying retinopathy long before its clinical manifestation and consequently optimizing its management. Our results also suggest that the arrangement of the more peripheral RBVA (most probably acquired traits) appears to be unique to one individual (even between monozygotic twins) and thus could be used as a biomarker in computerized identification systems. However, in doing so, one must also take into consideration that retinal diseases, epigenetics, trauma, and aging may alter the arrangement of the more peripheral RBVA.

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References

1. Köse C, İkibaş C. A personal identification system using retinal vasculature in retinal fundus images. *Expert Syst Appl*. 2011;38:13670–13681.

2. Qamber S, Waheed Z, Akram MU. Personal identification system based on vascular pattern of human retina. In: *2012 Cairo International Biomedical Engineering Conference (CIBEC)*. New York: Institute of Electrical and Electronics Engineers; 2012:64–67.

3. Simon C, Goldstein I. A new scientific method of identification. *N Y State J Med*. 1935;35:901–906.

4. Tower P. The fundus oculi in monozygotic twins; report of six pairs of identical twins. *AMA Arch Ophthalmol*. 1955;54:225–239.

5. Taarnhøj NC, Larsen M, Sander B, et al. Heritability of retinal vessel diameters and blood pressure: a twin study. *Invest Ophthalmol Vis Sci*. 2006;47:3539–3544.

6. Taarnhøj NC, Munch IC, Kyvik KO, et al. Heritability of cilioretinal arteries: a twin study. *Invest Ophthalmol Vis Sci*. 2005;46:3850–3854.

7. Healey P, Carbonaro F, Taylor B, Spector TD, Mitchell P, Hammond CJ. The heritability of optic disc parameters: A classic twin study. *Invest Ophthalmol Vis Sci*. 2008;49:77–80.

8. Drobnjak D, Taarnhøj NC, Mitchell P, et al. Heritability of optic disc diameters: a twin study. *Acta Ophthalmol Scand*. 2011;89:193–198.

9. Vergmann AS, Broe R, Kessel L, et al. Heritability of retinal vascular fractals: a twin study. *Invest Ophthalmol Vis Sci*. 2017;58:3997–4002.

10. Hughes S, Yang H, Chan-Ling T. Vascularization of the human fetal retina: roles of vasculogenesis and angiogenesis. *Invest Ophthalmol Vis Sci*. 2000;41:1217–1228.

11. Gauvin M, Chakor H, Koenekoop RK, Little JM, Lina JM, Lachapelle P. Witnessing the first sign of retinitis pigmentosa onset in the allegedly normal eye of a case of unilateral RP: a 30-year follow-up. *Doc Ophthalmol*. 2016;132:213–229.

12. Perez-Montaño CR, Palomares-Ordoñez JL, Ramirez-Estudillo A, Sanchez-Ramos J, González-Saldivar G. Sub-hyaloid and sub-internal limiting membrane macular hemorrhage after laser exposure at music festival: a case report. *Doc Ophthalmol*. 2019;138:71–76.

13. Hua Y, Voorhees AP, Sigal IA. Cerebrospinal fluid pressure: revisiting factors influencing optic nerve head biomechanics. *Invest Ophthalmol Vis Sci*. 2018;59:154–154.

14. Liew G, Wang JJ, Rochtchina E, Wong TY, Mitchell P. Complete blood count and retinal vessel calibers. *PLoS One*. 2014;9:e102230.

15. Karmakar B, Malkin I, Kobyliansky E. Inheritance of 18 quantitative dermatoglyphic traits based on factors in MZ and DZ twins. *Anthropol Anz*. 2011;68:185–193.

16. Loesch D. Genetics of dermatoglyphic patterns on palms. *Ann Hum Genet*. 1971;34:277–290.

17. Loesch D. Genetical studies of sole and palmar dermatoglyphics. *Ann Hum Genet*. 1974;37:405–420.

18. Huntzinger RS, Christian JC. The retinal blood vessel patterns in twins. *Prog Clin Biol Res*. 1978;24:241–246.