The Effect of Age on Optic Nerve Head Blood Flow

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PURPOSE. To examine whether optic nerve head blood flow changes with aging.

METHODS. One randomly chosen eye of each of 103 healthy subjects (age range, 22–76 years) was examined by laser Doppler flowmetry. Relative capillary blood flow, velocity, and volume of the moving red blood cells were measured at the temporal and nasal neuroretinal rim of the optic nerve head. For statistical analysis, linear regression analysis and partial correlations were calculated.

RESULTS. Velocity increased with age. The Pearson correlation coefficient (R) between age and velocity was 0.49 temporally and 0.56 nasally. The correlation was significantly different from 0 (both P < 0.0005). Volume decreased with increasing age. The Pearson correlation coefficient between age and volume was −0.47 temporally and −0.40 nasally. The correlation was significantly different from 0 (both P < 0.0005). Flow decreased with increasing age. The Pearson correlation coefficient between age and flow was −0.27 temporally and −0.31 nasally. The correlations were significantly different from 0 (P = 0.006 and P = 0.002, respectively). Partial correlation coefficients between the perfusion parameters and age, after correcting for systolic and diastolic blood pressure, heart rate, gender, and IOP, were similar compared to the Pearson correlation coefficients and remained statistically significant.

CONCLUSIONS. The perfusion of the optic nerve head is altered with increasing age. The results suggest that the blood supply is reduced in elderly subjects. (Invest Ophthalmol Vis Sci. 2005;46:1291–1295) DOI:10.1167/iovs.04-0987

In the process of aging, various organ systems are affected in the human body. With regard to the optic nerve head, histologic alterations have been described suggesting a vascular impairment with increasing age.1 As vascular risk factors (e.g., reduced perfusion of the optic nerve head (ONH)) may play a role in the pathogenesis of glaucoma2–4 and as glaucoma is more common in elderly than in younger individuals, it seems important to know how the perfusion of the ONH is affected by increasing age.

In vivo studies examining retrobulbar vessels, retinal, and choroidal perfusion showed a decrease of ocular perfusion with increasing age.5–8 However, the only study to examine the effect of aging on optic nerve head blood flow did not find a significant age effect.5

Therefore, the purpose of this study was to examine whether ONH blood flow is altered with increasing age.

SUBJECTS AND METHODS

Subjects

In a cross-sectional study, one randomly chosen eye of 103 healthy volunteers of different ages was examined. The subjects were recruited from persons accompanying patients and from staff, their friends, and their families. All subjects received an ophthalmic clinical examination, including evaluation of the optic disc showing no signs of glaucoma. Optic discs were considered normal if they had intact rims and no hemorrhages, notches, excavation, nerve fiber layer defects, or asymmetry of the vertical cup-to-disc ratio >0.2. None of the subjects had a history of increased intraocular pressure >21 mm Hg or was using topical medication. Subjects did not have cardiovascular disease and were not taking any systemic medication that might affect the vascular system (e.g., β-blockers, or calcium channel antagonists). In keeping with the tenets of the Declaration of Helsinki, written documentation of informed consent was taken and the study was explained to the subjects. The research was approved by the local ethics committee.

The age of the subjects ranged between 22 and 76 years (mean age, 42.5 ± 15.0). Sixty-six subjects were women and 37 were men.

Methods

The laser Doppler flowmeter (LDF; model 4000; Oculix Sarl, Arbaz, Switzerland) according to Riva was used for the blood flow measurements. The technical details of the instrument have been described in detail elsewhere.9 Briefly, this technique is based on the optic Doppler effect. Emitted laser light with a frequency of 670 nm is focused on the surface of the optic nerve head. The measured area has a diameter of approximately 160 μm. The coherent light is scattered by the moving red blood cells (RBCs) and the stationary tissue. The scattering caused by the RBCs leads to a frequency shift of the laser light. The scattering caused by the stationary tissue leads only to a randomization of the light directions striking the RBCs. The broadened spectrum of scattered laser light is subjected to spectral analysis. From this analysis the parameters velocity and volume are obtained. The parameter velocity represents the speed of the moving RBCs and the parameter volume corresponds to the amount of the moving RBCs. From these two parameters, the parameter flow is calculated representing the blood flow of the moving RBCs. These parameters represent relative, not absolute, values. Volume and flow are measured in arbitrary units [AU] and velocity in kilohertz.9 In a recent study, it was shown that approximately 25% of the measured signal originate from the deeper layers, which are supplied by the ciliary arteries (Boehm AG, et al. IOVS 1999;40:ARVO Abstract 779).

Before the examination, the pupil was dilated with 1 drop of tropicamide 1%. The measurements were performed in a darkened room. Measurements were taken at the nasal and temporal neuroretinal rim of the optic nerve head, away from visible vessels. For each measurement, during a period of several seconds, continuous recordings of the three parameters flow, volume, and velocity were obtained. As the recordings can be disturbed by events such as lid movements and head motion, a masked observer selected the part of the recording that showed a stable circulatory parameter. These parts of the measurements were used for the analysis.

Immediately after the flowmeter measurement, intraocular pressure was taken by applanation tonometry, and systemic perfusion parameters such as systolic and diastolic brachial arterial blood pressure and the heart rate were measured.
For statistical analysis, a Pearson correlation was calculated between perfusion parameters and age. Linear regression analysis was performed for the perfusion parameters implementing age, IOP, systolic and diastolic blood pressure, heart rate, and gender into the model. From this model, the change per 10 years with confidential intervals was calculated (slope of the regression line). The Sidak procedure was used to correct for multiple testing. To parse out the effect of age independent of systolic and diastolic blood pressure, heart rate, gender, and IOP, partial correlations between the perfusion parameters and age were performed, after correcting for systolic and diastolic blood pressure, heart rate, gender, and IOP.

For all statistics, \( P < 0.05 \) was considered to be statistically significant. All analyses were performed on computer (SPSS ver. 11.0; SPSS Science, Chicago, IL).

**RESULTS**

Velocity increased with age. The Pearson correlation coefficient \( R \) between age and velocity was 0.49 temporally and 0.56 nasally (Figs. 1, 2, respectively). This correlation was significantly different from 0 (both \( P < 0.0005 \)). The means (±SD) for velocity were 0.339 ± 0.104 AU temporally and 0.318 ± 0.107 AU nasally.

Volume decreased with age. \( R \) between age and volume was −0.47 temporally and −0.40 nasally (Figs. 3, 4, respectively; both \( P < 0.0005 \)). The means (±SD) for volume were 0.363 ± 0.193 AU temporally and 0.436 ± 0.286 AU nasally.

Flow decreased with age. \( R \) was −0.27 temporally and −0.31 nasally (Figs. 5, 6, respectively; \( P = 0.006 \) and 0.002, respectively). The means (±SD) for flow were 9.34 ± 2.11 AU temporally and 9.76 ± 3.48 AU nasally.

Linear regression analysis, examining the correlation between the perfusion parameters and age, systolic and diastolic blood pressure, heart rate, gender, and IOP showed a statistically significant correlation with age and IOP. The parameters diastolic and systolic blood pressure, heart rate, and gender did not show a significant correlation with either of the blood flow parameters. The results of the linear regression analysis are shown in Table 1. The partial correlation coefficients between
the perfusion parameters and age correcting for systolic and diastolic blood pressure, heart rate, gender, and IOP were similar compared to the Pearson correlation coefficients and remained statistically significant (Table 1).

The linear regression analysis showed a 10% increase per decade for temporal velocity and 11% for nasal velocity. Volume decreased temporally 14% and nasally 16% per decade, and blood flow decreased 4% temporally and 8% nasally (Table 2).

**DISCUSSION**

In this cross-sectional study the age dependence of blood flow measurements of the optic nerve head was examined. The results showed a significant correlation between age and the blood flow parameters velocity, volume, and flow. Age correlated positively with velocity and negatively with volume and flow. This observation was still present after taking other factors into account that might have influenced the measured perfusion parameters.

A possible explanation for this constellation of perfusion parameters is an increased resistance of the vascular bed of the optic nerve head in older subjects. An increase in resistance could be caused by a reduction in the functional total vessel diameter. Either the capillaries themselves have a smaller diameter or the density of the capillaries is decreased in older subjects compared with younger ones. Both possibilities would lead to a reduction in a total vessel diameter, with an increase in velocity and decrease in volume.

With a correlation coefficient $-0.31$ age seems to predict only 9% ($R^2$) of the nasal flow and with $-0.27$ only 7% of the temporal flow. The effect on velocity, however, was the strongest. The correlation coefficients suggest that 24% ($R^2$) temporally to 31% ($R^2$) nasally of the velocity change can be predicted by age. The effect on the volume was only 16% ($R^2$) temporally and 18% ($R^2$) nasally.

There is evidence that the blood flow of the optic nerve is autoregulated. To maintain a constant blood flow, vessel diameters are changed, altering velocity and volume. There-
fore, the different effect on the perfusion parameters due to age might be related to these regulative mechanisms.

The linear regression analysis showed that besides age, only IOP had an effect on the measured perfusion parameters as well. However, the effect of age on the perfusion parameters was the strongest.

Another factor that could affect measurements of blood flow parameters is the thickness of the superficial nerve fiber layer. It is known that there is a small but significant decrease in the number and density of retinal nerve fibers with age. This has been shown histologically but also with imaging devices (e.g., OCT; Carl Zeiss Meditec, Jena, Germany; or the GDx nerve fiber analyzer; Laser Diagnostic Technologies, Inc., San Diego, CA). However, in one study, it was shown that there is no significant correlation between perfusion parameters measured by scanning laser Doppler flowmetry and retinal nerve fiber layer thickness measurements performed with the nerve fiber analyzer. Measurements with the laser Doppler flowmeter performed according to Riva showed no correlation to retinal nerve fiber layer thickness measurements, (unpublished data, 1999). Therefore it seems to be unlikely that the small reduction in retinal nerve fiber layer thickness due to age is significantly responsible for the changes in blood flow parameters with increasing age.

Another important point one has to be aware of is the cross-sectional design of the study: No measurements of the same individuals at different ages were compared; instead measurements of different individuals were collected at different ages. The ideal study design to evaluate the age effect on the perfusion parameters is the thickness of the superficial nerve fiber layer. It is known that there is a small but significant decrease of retinal blood flow of 8% per decade, which is similar to the change of optic nerve head blood flow in our study.

In contrast to our study, the only previous report about the effect of age on optic nerve head blood flow by Groh et al. did not show significant effect. Possible reasons for this difference may be the smaller number of subjects and a different technique in their study. However, they reported a statistically significant decrease of retinal blood flow of 8% per decade, which is similar to the change of optic nerve head blood flow in our study.

In summary, the present study shows an alteration of the perfusion of the optic nerve head with increasing age, suggesting that the blood supply is reduced in elderly subjects.

**Acknowledgments**

The authors thank Eberhard Kuhlisch, PhD (Institute of Medical Statistics and Biometry, University of Dresden), for assistance with statistical analysis.

**References**

3. Drance SM. Primary chronic open angle glaucoma: are there vascular risk factors (in German)? *Klin Monatsbl Augenheilkd.* 1996; 208:A9–A15.

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**Table 1. Partial Correlations between Perfusion Parameters and Patient Characteristics**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Age</th>
<th>IOP</th>
<th>Gender</th>
<th>Systolic BP</th>
<th>Diastolic BP</th>
<th>Heart Rate</th>
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<tbody>
<tr>
<td>Temporal velocity</td>
<td>+0.47</td>
<td>-0.25</td>
<td>+0.11</td>
<td>-0.09</td>
<td>+0.18</td>
<td>+0.11</td>
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<tr>
<td>Nasal velocity</td>
<td>+0.48</td>
<td>-0.27</td>
<td>+0.13</td>
<td>+0.05</td>
<td>+0.03</td>
<td>+0.06</td>
</tr>
<tr>
<td>Temporal volume</td>
<td>-0.45</td>
<td>+0.34</td>
<td>-0.02</td>
<td>+0.13</td>
<td>-0.09</td>
<td>-0.22</td>
</tr>
<tr>
<td>Nasal volume</td>
<td>-0.38</td>
<td>+0.30</td>
<td>-0.03</td>
<td>-0.11</td>
<td>+0.01</td>
<td>-0.17</td>
</tr>
<tr>
<td>Temporal flow</td>
<td>-0.23</td>
<td>+0.19</td>
<td>+0.02</td>
<td>+0.05</td>
<td>+0.05</td>
<td>-0.20</td>
</tr>
<tr>
<td>Nasal flow</td>
<td>-0.33</td>
<td>+0.29</td>
<td>+0.01</td>
<td>-0.06</td>
<td>0.00</td>
<td>-0.16</td>
</tr>
</tbody>
</table>

Each parameter was correlated to the perfusion parameters, correcting for the other parameters.

† *P < 0.01.

* P < 0.005.

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**Table 2. Changes of the Perfusion Parameters per Decade**

<table>
<thead>
<tr>
<th>Change per 10 y</th>
<th>95% Confidence Interval</th>
<th>Change per 10 y (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temporal velocity</td>
<td>+0.035 kHz</td>
<td>+0.02 to +0.05 kHz</td>
</tr>
<tr>
<td>Nasal velocity</td>
<td>+0.035 kHz</td>
<td>+0.02 to +0.05 kHz</td>
</tr>
<tr>
<td>Temporal volume</td>
<td>-0.051 AU</td>
<td>-0.07 to -0.03 AU</td>
</tr>
<tr>
<td>Nasal volume</td>
<td>-0.071 AU</td>
<td>-0.11 to -0.04 AU</td>
</tr>
<tr>
<td>Temporal flow</td>
<td>-0.34 AU</td>
<td>-0.64 to -0.04 AU</td>
</tr>
<tr>
<td>Nasal flow</td>
<td>-0.80 AU</td>
<td>-1.30 to -0.31 AU</td>
</tr>
</tbody>
</table>

The left column shows the absolute change, the middle column shows the 95% confidence interval, and the right column shows the percentage change of the mean per 10 years.