Ocular Vasodynamic Changes in Light and Darkness in Smokers

Ulf Havelius1 and Flemming Hansen2

PURPOSE. To determine whether smokers have a reduced capacity for increased retinal blood flow velocity in darkness.

METHODS. The peak systolic flow velocities ($V_S$) and end diastolic flow velocities ($V_E$) were measured by ultrasound (i.e., color Doppler equipment), in light and darkness in the ophthalmic and central retinal arteries in 20 cigarette smokers and 20 matched nonsmokers. The resistive index ($RI$) was calculated as $RI = (V_E - V_S)/V_S$.

RESULTS. In the ophthalmic artery in nonsmokers, the $V_O$ was markedly increased in darkness and the $RI$ was correspondingly reduced. After the subject was re-exposed to light, the $RI$ was markedly increased. In smokers the $V_O$ and $V_S$ did not change significantly in the different conditions of light and darkness. In the central retinal artery in nonsmokers, the $V_O$ and $V_S$ were markedly increased in darkness and decreased after re-exposure to light. In smokers, the corresponding changes were much smaller and not significant.

CONCLUSIONS. The normal capacity for increased blood flow velocity in the central retinal artery in darkness was markedly reduced in smokers. This finding may explain the reduced dark vision after recent smoking reported in several studies and probably reflects the combined effects of an increased blood viscosity, the vasoconstrictive action of nicotine, and a reduced capacity of the blood to transport oxygen, as the hemoglobin is partly occupied by carbon monoxide. (Invest Ophthalmol Vis Sci. 2005;46:1698–1705) DOI:10.1167/ioves.04-0756

Only a few studies using color Doppler imaging (CDI) of the ocular circulation have been performed in chronic smokers,1–3 and the results have to some extent been ambiguous. Williamson et al.1 and Kaiser et al.2 found no differences between chronic smokers and nonsmokers in the flow velocities or resistive indices ($RI$s) of the central retinal artery, whereas Steigerwalt et al.3 showed reduced flow velocities and increased $RI$s in chronic smokers. Also the results of studies of chronic smokers and nonsmokers comparing dark vision have been partly contradictory. Most investigators have found reduced dark adaptation in connection with smoking,1–7 although a few reports suggest no impact on dark vision in smokers.8,9 The duration of the interval between smoking and dark adaptometry seems to be of relevance in explaining these discrepant results—that is, recent smoking more probably affects dark vision. We have demonstrated an increased flow velocity in the central retinal artery in response to darkness using CDI,10 and we now wanted to study whether recent smoking in chronic smokers is connected with a synchronous incapacity for increased flow velocity in the central retinal artery in response to darkness.

METHODS

Subjects

Twenty habitual cigarette smokers (8 men and 12 women; 20–54 years of age; mean, 36 years) who smoked 15 to 25 cigarettes a day, and 20 matched nonsmoking individuals (8 men and 12 women; 21–63 years of age; mean, 37 years) were examined by CDI. All participating individuals were anamnestically free of cardiovascular and neurologic diseases and took no medication. They were ophthalmically healthy (i.e., had normal vision, intraocular pressure [IOP], dark adaptation, and pupillary reactions).

In the chronic smokers the CDI examinations were performed immediately after the subjects had smoked three cigarettes during the preceding hour. On the contrary, dark adaptometry was made after an interval of at least 1 hour from most recent possibility to smoke a cigarette. Dark adaptometry was made to verify that smokers had normal dark adaptation if not under the acute influence of smoking.

Test Procedure

The test procedure was a modification of our previously described method.10 The sequential exposures to light and darkness were identical with the previously reported conditions, but the number of CDI registrations during each experiment was reduced from 7 to 3.

All subjects were identically examined by CDI while in a supine position, shielded from the monitor. The measurements were performed by an experienced laboratory technician. Blood flow velocities in the ophthalmic and central retinal arteries were measured in each pair of eyes three times (sessions 1, 2, and 3) under standardized conditions of light and darkness (Fig. 1). The right eye was always examined before the left. The subject kept the eye not being examined open, when the room was lit. The initial recording was performed in standardized light (120 lux in the position of the eyes; Fig. 1). Then the subject looked with both eyes into a 55-W lamp for 5 minutes from a distance of 20 cm (1350 lux in the position of the eyes), after which the monitor and the control panel were covered with red plastic film (027 medium red, BS 3944; Part 1, 1992; Lee Filters, Andover, UK; light transmission: 0% [600 nm], >50% [650 nm], and >80% [>700 nm]). All leaks of light were eradicated. The examination room was in complete darkness except for the red light emitted from the monitor and control panel. The subject kept both eyes closed during the period of darkness. Measurements in the right and left eyes were taken after 25 minutes of darkness. The light in the room was then turned on, the red filter was removed, and the third measurement of flow velocities in the right and left eyes was performed. The arterial blood pressure was measured three times during the test period (i.e., after each of the three CDI registrations was completed; Fig. 1).

Color Doppler Imaging

For the Doppler measurements we used identical equipment and method as previously reported.10 All ultrasound examinations were done with a commercial system (model XP 128; Acuson, Mountain View, CA) equipped with a 7-MHz linear array, real-time B-mode scan-
ner, including a 5-MHz pulsed and color Doppler (both modalities in this report are included in the abbreviation CDI). This type of instrumentation is commonly used for examinations of the orbit without causing any problems by inducing a temperature increase or other unwanted phenomena.11–13

At each registration, the peak systolic velocity ($V_S$) and end diastolic velocity ($V_D$) were measured14,15 and the resistive index ($RI$) was subsequently calculated16 as: $RI = (V_S - V_D)/V_S$.

**Carboxyhemoglobin**

During the hour preceding the CDI measurements, all smoking subjects smoked three cigarettes. A blood sample was then taken for analysis of the level of carboxyhemoglobin (COHb). In nonsmokers, no analysis of COHb was performed. The level of COHb in blood was measured spectrophotometrically by an automated and computerized blood gas analyzer (ABL 725; Radiometer, Copenhagen, Denmark) and results were given as a percentage of the total hemoglobin concentration.

**Statistical Methods**

The results are expressed as the mean ± SEM. In all calculations, the right and left sides were treated separately. Paired $t$-tests were used in nonsmokers and smokers to compare systolic and diastolic flow velocities, RIs, and systolic and diastolic arterial blood pressures under the different conditions of light and darkness. Unpaired $t$-tests were used to compare the same parameters between nonsmokers and smokers. Possible correlations were checked between the arterial blood pressure at the three registrations and the flow parameters and also between IOP and the flow parameters in the ophthalmic and central retinal artery on the same occasions. Possible correlations were also checked in smokers between the level of COHb and the various flow parameters at the three registrations. The basic level of significance was chosen as $P ≤ 0.05$. The Bonferroni method was used to minimize the influence of multiple comparisons. After adjustment the levels of significance were $P ≤ 0.017$ (comparison of the flow parameters at registrations 1 to 3; correlations for arterial blood pressure) and $P ≤ 0.006$ (correlations of COHb and IOP).

The study was approved by the Ethics Committee at the University of Lund. The subjects gave informed consent to participate, and all experimental procedures conformed to the tenets of the Declaration of Helsinki.

**RESULTS**

**Ophthalmic Artery**

In the ophthalmic arteries in nonsmokers, the mean predarkness $V_S$ (right eye: 45.4 cm/s; left eye: 44.5 cm/s) did not consistently change after 25 minutes in darkness or after re-exposure to light (Table 1; Fig. 2). In smokers the predarkness $V_S$ (right eye: 45.6 cm/s; left eye: 44.6 cm/s) was unchanged in the different conditions of light and darkness.

In nonsmokers the mean predarkness $V_S$ (right eye: 9.9 cm/s; left eye: 9.5 cm/s) increased significantly after 25 minutes in darkness (right eye: 14.0 cm/s, $P < 0.008$; left eye: 11.7 cm/s, $P = 0.006$) compared to the level of COHb (nonsmokers: 0.1% ± 0.2%; smokers: 0.5% ± 0.3%).

**Central Retinal Artery**

In smokers, the mean predarkness $V_S$ (right eye: 7.1 cm/s; left eye: 6.9 cm/s) increased significantly after 25 minutes in darkness (right eye: 7.7 cm/s, $P < 0.017$; left eye: 7.4 cm/s, $P = 0.008$) compared to the level of COHb (nonsmokers: 0.3% ± 0.4%; smokers: 0.5% ± 0.6%).

**TABLE 1. Flow Velocities in the Ophthalmic Artery and Central Retinal Artery in Nonsmokers and Smokers at Three Doppler Registrations**

<table>
<thead>
<tr>
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<th>Right Eye (Session)</th>
<th>Left Eye (Session)</th>
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<tbody>
<tr>
<td><strong>Ophthalmic artery</strong></td>
<td></td>
<td></td>
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<tr>
<td>Nonsmokers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSV</td>
<td>45.4 ± 3.0</td>
<td>45.4 ± 3.0</td>
</tr>
<tr>
<td>EDV</td>
<td>9.9 ± 0.9</td>
<td>14.0 ± 2.0</td>
</tr>
<tr>
<td>Smokers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSV</td>
<td>45.6 ± 2.2</td>
<td>45.4 ± 2.6</td>
</tr>
<tr>
<td>EDV</td>
<td>12.2 ± 1.0</td>
<td>13.9 ± 1.3</td>
</tr>
<tr>
<td><strong>Central retinal artery</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonsmokers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSV</td>
<td>7.1 ± 0.4</td>
<td>9.1 ± 0.5</td>
</tr>
<tr>
<td>EDV</td>
<td>1.9 ± 0.2</td>
<td>3.0 ± 0.2</td>
</tr>
<tr>
<td>Smokers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSV</td>
<td>6.9 ± 0.4</td>
<td>7.4 ± 0.4</td>
</tr>
<tr>
<td>EDV</td>
<td>1.8 ± 0.2</td>
<td>2.3 ± 0.2</td>
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Data are mean centimeters per second ± SEM. PSV, peak systolic velocity; EDV, end diastolic velocity.
cm/s, \( P < 0.003 \); Table 1; Fig. 2). After re-exposure to light, the mean \( V_D \) of the right eye was reduced to 12.3 cm/s (\( P < 0.002 \)). The corresponding change in the left eye in response to light was notably less marked and not significant. In smokers, the mean \( V_D \) was not significantly changed under the different conditions of light and darkness.

When the systolic and diastolic flow velocities in nonsmokers were compared with the corresponding values in smokers, no significant differences were found on any side at any of the three registrations (Table 1).

In nonsmokers, the mean predarkness RIs were significantly reduced after 25 minutes in darkness (Table 2). After re-exposure to light the RIs increased, but the levels were still considerably reduced compared with the predarkness levels. In smokers the mean predarkness RIs were significantly reduced after 25 minutes in darkness (Table 2). After re-exposure to light, the RIs essentially remained reduced. The RIs were higher before darkness in the nonsmokers than in the smokers (right eye: \( P = 0.05 \); left eye: \( P = 0.02 \)) but did not show any differences in either eye at the other two registrations.

**Central Retinal Artery**

In the central retinal arteries in nonsmokers, both the mean predarkness systolic and diastolic flow velocities increased markedly after 25 minutes in darkness and then decreased after re-exposure to light (Table 1; Fig. 3). The initial mean \( V_S \) increased in darkness in the right eye by 28% from 7.1 to 9.1 cm/s (\( P < 0.0001 \)) and in the left eye by 32% from 6.8 to 9.0 cm/s (\( P < 0.0001 \)). After re-exposure to light, the \( V_S \) was decreased in the right eye by 15% to 7.7 cm/s (\( P < 0.0001 \)) and in the left eye by 18% to 7.4 cm/s (\( P < 0.0001 \)). The mean \( V_D \) after 25 minutes in darkness increased in the right eye by 58% from 1.9 to 3.0 cm/s (\( P < 0.0001 \)) and in the left eye by 65% from 1.7 to 2.8 cm/s (\( P < 0.0001 \)). After re-exposure to light, the \( V_D \) decreased in the right eye by 27% to 2.2 cm/s
In smokers, there were similar but much less pronounced and nonsignificant changes in the systolic and diastolic flow velocities after 25 minutes in darkness and after re-exposure to light (Table 1; Fig. 3).

The systolic and diastolic velocities were also compared between nonsmokers and smokers at the three registrations (Table 1). No significant differences were noted between velocities before darkness and those after re-exposure to light. After 25 minutes in darkness, the systolic velocities were significantly higher in nonsmokers (right eye: \( P < 0.005 \); left eye: \( P < 0.005 \)).

### TABLE 2. Comparison of Resistive Index in the Ophthalmic Artery in Nonsmokers and Smokers at Three Doppler Registrations

<table>
<thead>
<tr>
<th></th>
<th>Right Eye (Session)</th>
<th>Left Eye (Session)</th>
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<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Nonsmokers</td>
<td>0.78 ± 0.02</td>
<td>0.70 ± 0.02</td>
</tr>
<tr>
<td>( P (1 \text{ vs. } 2 \text{ and } 2 \text{ vs. } 3) )</td>
<td>(&lt;0.0001)</td>
<td>(&lt;0.0004)</td>
</tr>
<tr>
<td>( P (1 \text{ vs. } 3) )</td>
<td>(&lt;0.0008)</td>
<td>( \text{NS} )</td>
</tr>
<tr>
<td>Smokers</td>
<td>0.73 ± 0.02</td>
<td>0.70 ± 0.02</td>
</tr>
<tr>
<td>( P (1 \text{ vs. } 2 \text{ and } 2 \text{ vs. } 3) )</td>
<td>(&lt;0.003)</td>
<td>( \text{NS} )</td>
</tr>
<tr>
<td>( P (1 \text{ vs. } 3) )</td>
<td>( \text{NS} )</td>
<td>( \text{NS} )</td>
</tr>
</tbody>
</table>

Data are the mean ± SEM.

\( (P < 0.001) \) and in the left eye by 16\% to 2.3 cm/s \( (P = 0.06) \).

In smokers, there were similar but much less pronounced and nonsignificant changes in the systolic and diastolic flow velocities after 25 minutes in darkness and after re-exposure to light (Table 1; Fig. 3).
The level of COHb in the smokers ranged between 3.8% and 9.9%, (mean, 5.84% ± 0.34%). There were no statistically significant linear correlations between the level of COHb and the flow velocity parameters at the three registrations in the ophthalmic or the central retinal artery.

**Arterial Blood Pressure**

In both nonsmokers and smokers, systemic arterial blood pressure was compared among the three registrations (Table 4). No significant changes were found among the nonsmokers. Smokers had a small but significant reduction between the predarkness systolic blood pressure and the pressure after re-exposure to light (P < 0.006). Diastolic blood pressure was reduced in the smokers between sessions 1 and 2 (P < 0.02) and also between sessions 1 and 3 (P = 0.02). No other significant changes were recorded among smokers.

Systolic and diastolic blood pressures were also compared between nonsmokers and smokers at the three registrations. No significant differences were found.

The calculations of possible correlations between systemic systolic and diastolic arterial blood pressures at the three registrations and the various flow parameters in the ophthalmic and central retinal artery on the same occasions did not reveal any conclusive findings in neither nonsmokers nor smokers.

**Carboxyhemoglobin**

The level of COHb in the smokers ranged between 3.8% and 9.9%, (mean, 5.84% ± 0.34%). There were no statistically significant linear correlations between the level of COHb and the flow velocity parameters at the three registrations in the ophthalmic or the central retinal artery.

### Intraocular Pressure

IOP was measured once in every individual. The mean levels were virtually identical in nonsmokers and smokers and in right and left eyes (Table 5). There were no conclusively significant linear correlations in nonsmokers or smokers between IOP and the various flow parameters in the ophthalmic and central retinal artery at any of the three registrations.

**DISCUSSION**

This study was performed in selected healthy subjects: habitual smokers and nonsmokers. The results should therefore reflect the physiological differences between the two groups in ocular blood flow velocity in the transition from light to darkness and vice versa. However, the results from the first of our three registrations should be comparable with other studies that have used CDI to investigate the influence of smoking on the ocular circulation. For the central retinal artery our results are in agreement with those of Williamson et al., who examined both eyes in 65 smokers and 249 nonsmokers and did not find any differences between the two groups when comparing the systolic and diastolic flow velocities or the RIs. Steigerwalt et al. examined both eyes in 10 smokers and 11 nonsmokers and found lower systolic and diastolic flow velocities and higher RIs in smokers than in nonsmokers. In the ophthalmic artery, we found significantly lower RIs in smokers, in agreement with the results of Williamson et al. and Kaiser et al., but not with Steigerwalt et al., who found no difference in RIs between smokers and nonsmokers.

CDI was used in our previous and present studies. There are certain advantages to CDI compared with laser Doppler velocimetry when examining ocular flow velocity in light and darkness. The problem of the laser beam’s causing illumination of the retina is avoided. The examination can be performed in complete darkness with the subject’s eyes closed (with the weak light sources in the room covered by a red filter). Repeated examinations can be performed. There is no need for strict visual fixation by the subject. One disadvantage with the CDI technique is the possibility that IOP may be increased by the gentle pressure of the probe on the globe.

### Table 3. Comparison of Resistive Index in the Central Retinal Artery in Nonsmokers and Smokers at Three Doppler Registrations

<table>
<thead>
<tr>
<th></th>
<th>Right Eye (Session)</th>
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<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Nonsmokers</td>
<td>0.73 ± 0.02</td>
<td>0.67 ± 0.02</td>
</tr>
<tr>
<td>P (1 vs. 2 and 2 vs. 3)</td>
<td>&lt;0.01</td>
<td>NS</td>
</tr>
<tr>
<td>Smokers</td>
<td>0.74 ± 0.02</td>
<td>0.70 ± 0.02</td>
</tr>
<tr>
<td>P (1 vs. 2 and 2 vs. 3)</td>
<td>NS (0.1)</td>
<td>NS</td>
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<tr>
<td>P (1 vs. 3)</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

Data are the mean ± SEM.

### Table 4. Arterial Blood Pressure in Nonsmokers and Smokers at Three Doppler Registrations

<table>
<thead>
<tr>
<th></th>
<th>Nonsmokers (Session)</th>
<th>Smokers (Session)</th>
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<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Systolic</td>
<td>117 ± 5</td>
<td>115 ± 4</td>
</tr>
<tr>
<td>Diastolic</td>
<td>71 ± 3</td>
<td>71 ± 2</td>
</tr>
</tbody>
</table>

Data are mean mm Hg ± SEM.
In our previous study, there was no significant increase in VD in the ophthalmic artery in 12 healthy subjects after 25 minutes in darkness. In the present study, the same measure was markedly increased bilaterally in the 20 nonsmokers. This finding is probably an expression of the higher number of subjects, making the previously insignificant increase in VD in darkness more evident and statistically significant. The change in the number of CDI registrations should not have any impact on the results, as the fundamental experimental conditions of light and darkness are identical in the previous and the present study.

Our previous study demonstrated progressively increased systolic and diastolic flow velocities in the central retinal artery with time spent in darkness. The finding was not explained by any dark-induced changes of arterial blood pressure, IOP, blood viscosity, or lumen diameter of the central retinal artery but instead by a decrease in peripheral retinal resistance.

The normal increase in systolic and diastolic flow velocities in darkness in the central retinal artery may reflect an increased metabolic demand of the photoreceptors. Experimental studies in animals have shown that darkness is accompanied by a markedly increased oxidative metabolism in the retinal photoreceptors and consequently, dark vision is critically dependent on a sufficient oxygen supply. How do these circumstances explain the normal increase of flow velocity in darkness in the central retinal artery? The retina has a dual vascular supply: the retinal arteries and the choroidal circulation. The contribution of oxygen from each of these sources at different retinal depths depends on conditions of light and darkness. The oxygen derived from the choroid reaches the inner segments of the photoreceptors independent of light conditions. In darkness, the photoreceptors have a markedly raised oxidative metabolism, and, consequently, the amount of oxygen diffusing from the choroid into the retina beyond the photoreceptors is reduced. Because the inner retina maintains its oxidative metabolism irrespective of light and dark, the oxygen tension in the inner retina decreases in darkness and triggers an increased retinal blood flow by mechanisms of autoregulation.

In the present study, we used the finding that darkness causes increased flow velocity in the central retinal artery as a “provocation test” and applied it to smokers and matched control subjects.

The test procedure entailed a modification of our previously described method, as regards the number of CDI registrations during each experiment. The sequential conditions of light and darkness were the same as previously, however, and consequently, the physiological conditions were identical in the present and the previous experiments at the three times when the CDI measurements were performed.

Ophthalmic Artery

The fact that in nonsmokers the VD in the ophthalmic artery was increased in darkness and reduced after re-exposure to light while there were no conclusive changes in the VD may be a reflection of the orbital vascular conditions. The ophthalmic artery has a larger lumen diameter and considerably higher systolic and diastolic flow velocities than the central retinal artery. According to the normal vascular anatomy of the orbita, the flow velocity in the ophthalmic artery was measured distal to the branching off of the central retinal artery. Consequently, even marked changes in the flow velocities in the central retinal artery may not be accompanied by statistically significant flow velocity changes in the ophthalmic artery. If such secondary changes should occur, it would most likely be manifested at the diastolic level. In addition, the reduced need for retinal “cooling” reduces the choroidal flow in darkness, which may contribute to a lower flow velocity in the ophthalmic artery, further confounding the interpretation of flow velocity changes in the ophthalmic artery in light and darkness.

Smokers in darkness had an insignificant increase in VD in the ophthalmic artery, which after re-exposure to light was strongly reduced in smokers. This may reflect that the adaptation to darkness and possibly the subsequent readaptation to light is slower in smokers than in nonsmokers. Such an interpretation is supported by the fact that some investigators have not found any differences in dark adaptation between smokers and nonsmokers. These studies characteristically seem to have had an extended interval between smoking and dark adaptometry. A delayed dark adaptation, which reaches the normal level after a prolonged interval, may explain the differences between studies as regards the influence of smoking on dark adaptation. In nonsmokers the systolic and diastolic flow velocities in both eyes did not return to baseline after re-exposure to light (Fig. 3). We have observed this phenomenon previously and believe it reflects a rather slow de-adaptation process, for which the time course of the possibly accompanying change in flow is unknown. Smokers, after a nonsignificant increase in systolic and diastolic flow velocity in darkness, essentially remained on the slightly elevated level after re-exposure to light. This may be an expression of the same phenomenon.

Why is the capacity to increase flow velocity in the central retinal artery in response to darkness strongly reduced in smokers? The reason may be the influence on factors of relevance for flow velocity (i.e., arterial blood pressure, IOP, blood viscosity, lumen diameter of the blood vessel, and peripheral resistance).

An increased mean arterial blood pressure would theoretically be an explanation for the normal increase in flow velocity in the central retinal artery in darkness. However, in nonsmokers, both the systolic and diastolic arterial mean blood pressures remained on virtually the same levels during the whole experiment (Table 4). In smokers, the systolic arterial mean blood pressure was successively and slightly reduced at the
three registrations, whereas the mean diastolic blood pressure decreased somewhat after 25 minutes in darkness. Consequently, the changes in flow velocities cannot be ascribed to variations in systemic blood pressure.

A decrease in IOP would be another possible explanation for the normally increased flow velocity in the central retinal artery in darkness recorded in nonsmokers. However, darkness normally induces an increase in IOP amounting to a few millimeters of mercury. This increase is not caused by any change of the pupilary diameter but may be due to changes in vasoregulation. It is known that artificial elevation of IOP by suction cup dynanometry in normal eyes results in progressive reduction of velocity with increasing IOP. However, in normal eyes Gutholf et al. found no correlation between the systolic flow velocity in the central retinal artery and the IOP. Consequently, the normal increase of flow velocity in the central retinal artery found in nonsmokers in darkness cannot be explained by any expected change of the IOP in darkness.

Can the strongly reduced flow velocity response to darkness in the central retinal artery in the smokers be explained by a change in IOP? Some investigators have found a weak association between current smoking and an increased IOP. All subjects in our study had normal IOPs and there were no differences in mean levels of IOP between smokers and non-smokers in either eye (Table 5). As studies of the acute effects of smoking have shown any impact on IOP the reduced capacity in smokers to increase flow velocity in the central retinal artery in darkness cannot be explained by any expected change of IOP in darkness.

Changed blood viscosity can reasonably be excluded as a factor explaining the increased flow velocity in darkness in nonsmokers, considering the short duration of the experiments. However, it is well documented that smoking has hemorheologic consequences. It leads to a rise in hematocrit and increases both fibrinogen levels and plasma viscosity. Smoking also alters the rheologic behavior of red blood cells. Together these changes cumulate in an increased whole blood viscosity and results in a significant deterioration of flow properties.

Changes in the lumen diameter of the examined vessel affect blood flow velocity, provided that all other parameters (e.g., perfusion pressure, blood viscosity) remain constant. The possible variation, between light and darkness in the lumen caliber of the central retinal artery at the position of repeated CDI measurements is not known. Information about changes in the caliber of the retinal arteries in light and darkness is sparse in the literature. Feke et al. and Barscay et al. each reported a negligible dilatation of larger branch retinal arteries in humans in darkness, whereas Hill and Houseman did not find any conclusive changes in the caliber of retinal arterioles between light and darkness in the cat.

Assuming that luminal changes in the central retinal artery between light and darkness are minor, the only possible interpretation of the increased flow velocity in nonsmokers is that there is a decrease in peripheral retinal vascular resistance in darkness. The decline in the RI (Table 3), derived to reflect variations in peripheral vascular resistance, supports such an interpretation.

The inhalation of cigarette smoke is invariably accompanied by the body’s taking up carbon monoxide (CO), which displaces oxygen from hemoglobin. CO competes with oxygen for binding at the iron-porphyrin centers of hemoglobin. These centers bind CO reversibly, but with an affinity >200 times greater than that for oxygen. The oxygen affinity of heme not occupied by CO is also increased in the presence of COHb, which impairs the release of oxygen to the tissues. These two effects of CO on hemoglobin decrease the partial pressure of oxygen in the tissues, which, depending on the degree, may result in tissue hypoxia with functional consequences for organ systems that require a continuous supply of oxygen.

Nicotine and CO, which are absorbed during smoking, have contrasting vasoactive properties. Nicotine produces constriction of the peripheral vasculature and increases the peripheral resistance to flow and hence the RI. CO is a cerebral vasodilator, complicating the interpretation of the combined effects of smoking on the retinal circulation. Our finding in nonsmokers of bilaterally significantly reduced RIs in darkness (Table 3), and corresponding nonsignificant changes in smokers, strongly supports the interpretation that nicotine is the dominant vasoactive factor. Furthermore, nicotine has a shorter half life (~2.6 hours) than CO (~4–5 hours), which is in better agreement with the limited duration of the influence of smoking on dark vision.

According to the Hagen-Poiseuille law, raised blood viscosity reduces blood flow unless compensated by vasodilation. Consequently, we interpret the reduced capacity in smokers for the increase in flow velocity in darkness to be a combination of increased blood viscosity and nicotine-induced constriction of the retinal circulation.

In summary, the normal capacity for the increase in flow velocity in the central retinal artery in darkness is strongly reduced in smokers. This effect is probably explained by the combined effects of increased blood viscosity and the vasoconstrictive action of nicotine. Synchronously, the impaired release of oxygen to the tissues caused by the binding of CO to hemoglobin further compromises the microenvironmental retinal conditions, creating a state of relative tissue hypoxia. As the increased metabolic demand by the photoreceptors in darkness is not met by a sufficient increase in supply, these conditions probably explain the reduced dark vision after recent smoking reported by several investigators on the subject.

Acknowledgments

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References


