

Nocturnal Dip in the Optic Nerve Head Perfusion

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Purpose: Many physiological parameters, including blood pressure, show circadian variations. Diurnal fluctuations of the optic nerve head (ONH) circulation have not yet been studied. The purpose of the present study was to determine the pattern of ONH blood flow variations over a 24-hour period in healthy subjects.

Methods: The subject group comprised 15 healthy volunteers (6 women, 9 men) aged 22 to 43 years (mean \pm SEM: 28.2 \pm 1.3 years). Blood flow in the ONH was measured by laser Doppler flowmetry (LDF) over a 24-hour period at 08:00, 12:00, 16:00, 20:00, 24:00 hours, and at 08:00 hours the following morning.

Results: ONH perfusion varied significantly over time. The mean LDF-flow during daytime ranged from 8.2 to 8.9 arbitrary units (AU) and fell at midnight to 7.1 AU ($P = .0015$). The mean LDF-volume during daytime was 0.23 to 0.24 AU and decreased at midnight to 0.20 AU ($P = .04$). The mean LDF-velocity ranged from 0.39 to 0.41 kHz with no significant differences at any time point.

Conclusions: Our study in normal subjects reveals small mean changes of ONH perfusion during daytime and a significant reduction at night. The physiological and clinical relevance of the nocturnal dip in the ONH perfusion needs to be determined in future studies. **Jpn J Ophthalmol 2000;44:128–131** © 2000 Japanese Ophthalmological Society

Key Words: Circadian variations, laser Doppler flowmetry, normal subjects, optic discs.

Introduction

The circadian modulation of waking and sleep has a profound impact on several physiological parameters, including, inter alia, brain activity, changes in the serum concentration of several hormones,^{1,2} changes in blood pressure,¹ renal K⁺ excretion.³ Diurnal variations of the optic nerve head (ONH) perfusion have not yet been studied.

Knowledge about such variations is, however, important both for basic eye physiology and understanding the pathophysiology of glaucoma^{4,5} and ischemic disorders of the ONH.^{6,7} Diurnal perfusion fluctuations may play a role in these diseases. The purpose of this study was to determine the pattern of the ONH perfusion variations in healthy volunteers over a 24-hour period.

Materials and Methods

Subjects

Blood flow in the ONH was measured by laser Doppler flowmetry (LDF) in 15 healthy volunteers (6 women, 9 men) aged 22 to 43 years (mean \pm SEM: 28.2 \pm 1.3 years). All subjects were nonsmokers, did not suffer from ocular or systemic diseases, and their refractive errors were within ± 3 diopters. Informed consent was obtained from all subjects. The pupil of one eye was dilated with tropicamide eye drops, and blood pressure (sphygmomanometry) and pulse rate were taken before every LDF measurement. LDF measurements were taken over a 24-hour period at 08:00, 12:00, 16:00, 20:00, 24:00 hours, and at 08:00 hours the following morning. Before each measurement, the subject was obliged to rest in the seated position in front of the LDF flowmeter for at least 20 minutes.

Laser Doppler Flowmetry in Optic Nerve Head

For examination, the probing laser beam of the LDF instrument (Oculix SARL, Arbaz, Switzerland)

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Table 1. Diurnal Variations in Perfusion of Optic Nerve Head as Measured by Laser Doppler Flowmetry (LDF)

Time of Day (hours)	Blood Pressure (mm Hg)		Pulse (bpm)	Flow (AU)	Volume (AU)	Velocity (kHz)
	Systolic	Diastolic				
08:00 [†]	122 ± 2	79 ± 2	73 ± 2	8.8 ± 0.4	0.24 ± 0.01	0.40 ± 0.01
12:00	116 ± 3	75 ± 3	69 ± 2	8.2 ± 0.3	0.23 ± 0.01	0.39 ± 0.02
16:00	123 ± 3	78 ± 3	71 ± 3	8.5 ± 0.4	0.23 ± 0.01	0.41 ± 0.02
24:00	122 ± 2	78 ± 2	70 ± 3	7.1 ± 0.4	0.20 ± 0.01	0.40 ± 0.02
08:00 [‡]	118 ± 2	74 ± 2	71 ± 2	8.9 ± 0.4	0.24 ± 0.01	0.40 ± 0.01

Note dip in flow and volume at midnight, and no obvious changes in velocity, systemic blood pressure, or pulse rate. See text for statistical evaluation of data. AU: arbitrary units.

*Mean ± SEM ($n = 15$) of LDF-flow, LDF-volume, and LDF-velocity as well as of blood pressure and pulse.

[†]First time point.

[‡]Last time point, 24 hours after first.

was positioned at the temporal rim of the optic disc in an area without visible vessels. In any given individual, the same position was utilized for all measurements. The emergent light-collecting fiber was aimed to overlap the laser spot.⁸

ONH perfusion is expressed by the following LDF variables: “velocity,” “volume,” and “flow.” LDF-velocity, expressed in kHz, is the mean of the frequency shift of the Doppler spectrum and is related to the mean velocity of blood cells in the sample volume of tissue. LDF-volume, expressed in arbitrary units (AU), is the power of the Doppler frequency shift spectrum and is proportional to the number of moving blood cells. LDF-flow, also expressed in AU, is proportional to the product of LDF-velocity and LDF-volume.⁹ Each measurement was recorded for about 90 seconds and the computer calculated the aforementioned variables every 50 milliseconds. The 90-second period was divided into three time segments. For each segment, 250 measurements were averaged, and these means were included in the statistical analyses. Thus each LDF recording yielded 3 means for each of the 3 flow variables. This approach was used to reduce the influence of short time flow fluctuations on the results.

Statistics

Effects of daytime on the variables LDF-flow, LDF-volume, LDF-velocity, blood pressure, and pulse rate were evaluated by analysis of variance (ANOVA) with repeated measurements. Effects of blood pressure and pulse on LDF-flow, LDF-volume, and LDF-velocity were evaluated by multivariate analysis of covariance (MANCOVA). A probability of $P \leq .05$ was regarded as significant. A post-hoc analysis of the differences among the means at the

different daytime points was performed by the Tukey honest significant difference test. The sample size estimation of LDF-velocity to obtain a significant difference between the smallest and the greatest group mean (based on the present data) was calculated with a power estimation for $\beta = 0.8$ and $\alpha = 0.05$.

Results

We found significant effects of time on LDF-flow and LDF-volume. Mean LDF-flow varied between 8.2 and 8.9 AU during the daytime and fell to 7.1 AU at midnight (Table 1). The midnight value differed significantly from the values at 08:00 ($P = .0034$), 16:00 ($P = .028$), 20:00 ($P = .032$), and at 08:00 ($P = .00153$) on the following day. Mean LDF-volume ranged between 0.23 and 0.24 AU during the daytime and fell to 0.20 AU at midnight (Table 1). The midnight value differed significantly from that at 08:00 ($P = .021$) on the following day. LDF-flow and LDF-volume exhibited a similar pattern (Figure 1) with respect to the nocturnal dip.

Mean LDF-velocity ranged from 0.39 to 0.41 kHz (Table 1) with no significant variations at any time ($P = .90$). Based on the present data, 131 observations would be required to find any significant differences in LDF-velocity.

Mean systolic blood pressure varied significantly and was lowest at noon ($P = .024$) (Table 1). In the analysis of covariance no significant effects of either blood pressure or pulse rate on LDF-flow, LDF-volume, or LDF-velocity were revealed.

Discussion

The present study was designed to determine circadian variations of the blood flow in the ONH. The

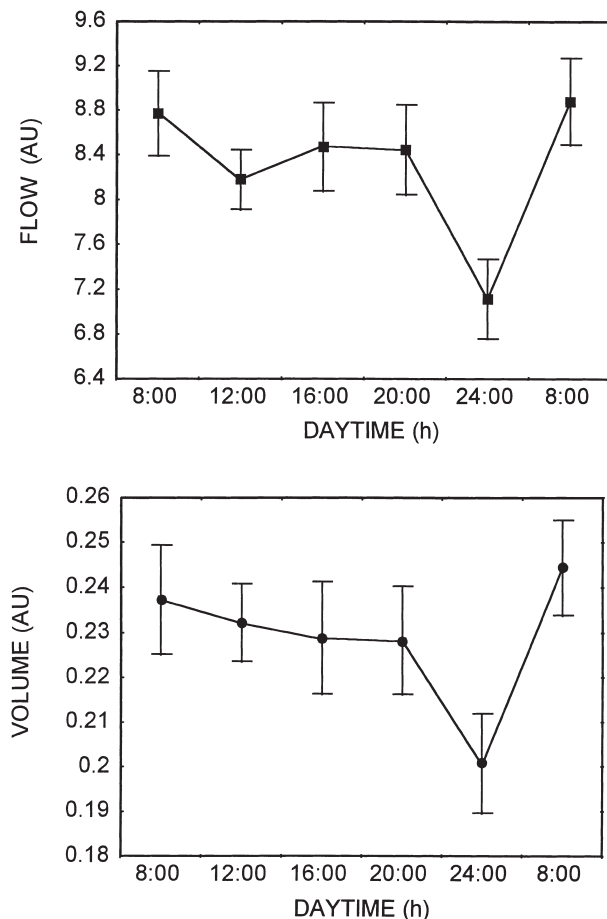


Figure 1. Diurnal variations of laser Doppler flowmetry (LDF)-flow and LDF-volume in optic nerve head. Note similar circadian pattern with dip at midnight. AU: arbitrary unit, ■ and ●: mean of measurements in 15 healthy volunteers. I: mean & SE, mean – SE.

results show a relatively constant flow during the daytime and a statistically significant drop in perfusion at midnight. Reduction in LDF-volume rather than in LDF-velocity seems to be responsible for the observed flow dip. Because we found a significantly lower flow at midnight, we presuppose that the ONH perfusion during the night differs from that during the day. To our knowledge this is the first report on diurnal variations in the ONH blood flow.

We attempted to maintain constant conditions for all LDF-recordings by obliging the subjects to rest before each measurement, and by making all recordings in a precisely defined area of the optic disc. So what could be the cause of the observed dip at night? ONH flow is affected by vasculo-hormonal factors^{6,7,10} as well as by physiological stimuli, such as flickering light that increases ONH blood flow.^{11,12} Blood pressure

physiologically drops at night,^{5–7,13} a potential factor in the pathogenesis of certain types of glaucoma and ischemic ONH diseases. However, a simple blood pressure–ONH-flow relationship refutes the fact that the ONH-perfusion is at least partially autoregulated and is expected to remain constant over a certain range of blood and eye pressure.¹⁰ This is supported by results of this study because blood pressure did not correlate with the LDF-flow.

Light also is unlikely to be the cause of the presently reported differences, because all subjects were exposed to a similarly attenuated light of the LDF fundus camera during each examination. The variations seem rather to result from the endogenous regulation of the ONH flow.

Our subjects had to be awakened for the midnight measurement. Waking raises blood pressure,^{14,15} as the result of increased sympathetic activity. Increased sympathetic activity, however, does not change the ONH-flow.¹⁰ Nevertheless, we cannot exclude an artifact due to the interruption of sleep. Determination of sympathetic activity as the cause for the nocturnal dip in ONH perfusion requires measurement of flow during an undisturbed sleep. For obvious technical reasons, this is not currently feasible.

Taken together, the presented literature does not explain our finding of a nocturnal perfusion dip. Therefore we postulate a circadian fluctuation in the ONH blood flow similar to those observed in other microcirculatory beds.^{16,17}

In conclusion, our study in normal subjects shows no significant changes of ONH perfusion during the daytime, whereas a flow dip at night is indicated. Further studies are needed to evaluate the physiological and clinical significance of this finding.

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