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Mathematical procedures in data recording and processing of pupillary fatigue waves

Holger Lüdtke [a,*], Barbara Wilhelm [a], Martin Adler [a], Frank Schaeffel [a], Helmut Wilhelm [a]

[a] *Universität-Augenklinik Tübingen, Abt. für Pathophysiologie des Sehens und Neuroophtalmologie, Schleichstr 12–16, 72076 Tübingen, Germany*

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Abstract

Spontaneous pupillary behaviour in darkness provides information about a subject's level of vigilance. To establish infrared video pupillography (IVP) as a reliable and objective test in the detection and quantification of daytime sleepiness, the definition of numerical parameters is an important precondition characterising spontaneous pupil behaviour adequately for further statistical procedures. The correct measurement of the pupil size, even if the lid or eyelashes are occluding the pupil, is of particular concern when testing vigilance. In this case many edge points of the pupil are detected and a fitting procedure is described that fits these edge points to a circle and excludes outliers. The first step of data preparation consists of a mathematical artefact management consisting of blink detection and elimination, followed by interpolation. Second, a fast Fourier transformation is carried out for frequencies from 0.0 to 0.8 Hz for each time segment of 82 s. Results are given in absolute and relative power of each frequency band per time segment and mean values over the entire record of 11 min. Third, the changes of the mean pupillary diameter per data window against time are shown graphically. An additional parameter referring to the pupil's tendency to instability, the pupillary unrest index (PUI), is defined by cumulative changes in pupil size based on mean values of consecutive data sequences. These mathematical procedures provide a high level of quality in both data collection and evaluation of IVP as an objective test of vigilance. In a pilot study, the pupillary behaviour of two groups were measured. One group rated themselves as alert (ten men), the other group as sleepy (12 men). The power and PUI were compared using the Mann–Whitney *U*-test. Both parameters show significant differences between the two groups. © 1998 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Spontaneous pupillary behaviour in darkness shows characteristic changes in excessive daytime sleepiness: in a drowsy subject, slow oscillations with increasing amplitude (fatigue waves, [1]) dominate and pupil diameter decreases continuously; while in an alert subject pupil size remains stable for a long time, oscillating mainly with a frequency of ≈ 1 Hz and amplitudes rarely exceeding 0.3 mm.

Infrared video pupillography (IVP) combined with a special image processing and analysing software offers the possibility of stable long time record of pupil size and accommodation and detailed analysis of changes of average pupillary diameter and spontaneous pupillary oscillations. The purpose of this paper is to describe and evaluate a procedure of pupillary measurement and data analysis, that allows one to gain numerical values describing spontaneous pupillary oscillations in order to introduce this as an universally applicable method to measure sleepiness.

2. Methods

2.1. Infrared video pupillography (IVP)

2.1.1. Instrument design

The subject is sitting in a comfortable chair, looking in a dark box and fixating an array of IR-LEDs which serve to illuminate the pupil. The IR-LEDs are placed

* Corresponding author. Tel.: +49 7071 2987097; fax: +49 7071 295361; e-mail: holger.luedtke@uni-tuebingen.de

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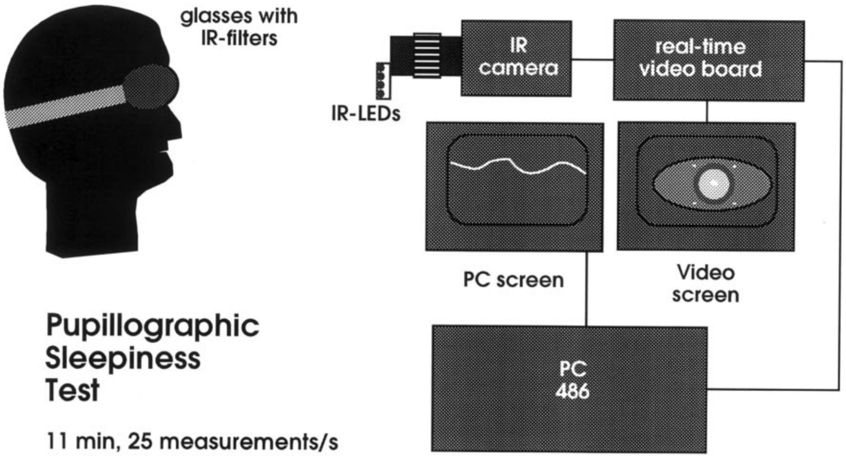


Fig. 1. Instrumental design. The subject is sitting in a comfortable chair fixating IR-LEDs. The image of the pupil is recorded by an IR-sensitive CCD-camera and analysed via a real-time video board with a PC. Diameter of the pupil, refraction and vergence are displayed on screen. Another screen shows the image of the pupil.

in front of the eyes at a distance of ≈ 0.8 m and are arranged confocally. The image of the bright pupil is recorded by an IR-sensitive CCD camera. To analyse the image of the pupil, we use a real-time video board CORECO Oculus 300 in a 486 PC (Fig. 1). The measured parameters, diameter of the pupil, horizontal and vertical vergence and refraction, are displayed for 11 min on-line on a screen with a sampling frequency of 25 Hz. On another screen, the image of the pupil is displayed.

The on-line record of accommodation and vergences ensures that a given change in pupil size really is spontaneous and enables the exclusion of movements related to the near reaction. At the same time, unstable fixation can be detected easily.

2.1.2. Detection of edge points of the pupil

Because of the confocal arrangement, the pupil image appears bright. At first, the brightest spot, the first Purkinje reflex, is detected. The left and right edge of the pupil is found by a horizontal line through the Purkinje reflex. Starting at the middle of this line (which should be a first approximation of the horizontal coordinate of the centre of the pupil) the upper and lower edge are measured. Before detecting these four points with a simple edge detection, the Purkinje reflex has to be cut off, otherwise the edges detected would be the edges of the Purkinje reflex and not of the pupil.

The vertical line is divided into several sections. At each intersection the left and right edges are detected (Fig. 2). For faster detection of these edge points, a threshold is defined from the four points measured at the beginning. The threshold is defined as a certain brightness that is darker than the brightness of pixels within the pupil and brighter than pixels outside the pupil. Especially because of eyelashes, the edge is not defined as the first point below this threshold. The next pixels are analysed, too, in order to continue with the search of the edge of the pupil if the next pixels are brighter than the threshold.

2.1.3. Fitting procedure

Having detected these data points, a circle (which should represent the pupil well enough) is fitted to these points. To reduce the effect of outliers, a second weighted fit is made. During the first fit, the weight of all data points is 1.

The fit is the minimisation of the following modified sum of square error function

$$J = \sum_{i=1}^{N} w_i \cdot [(x_i - x_0)^2 + (y_i - Y_0)^2 - r_0^2]^2 = \min.$$

where w_i: weight of ith data point; x_i, y_i: ith data point; x_0, y_0, r_0: optimal centre and radius.

As shown by Chaudhuri and Kundu [2] (even for weighted circular fits in a multidimensional space) this minimisation problem can be solved in a closed form:

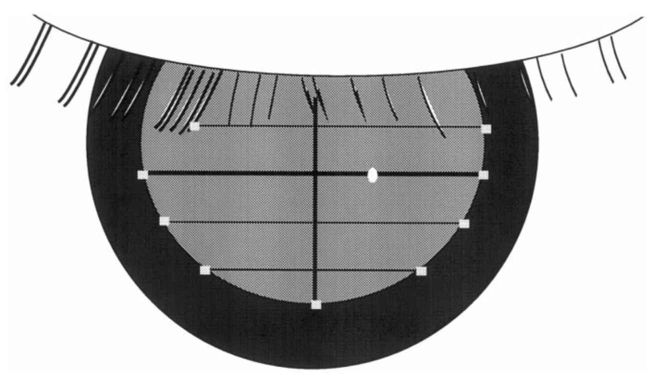


Fig. 2. Measurement of pupil. After searching the Purkinje reflex a horizontal scan detects the right and left edge of the pupil. From the centre of the horizontal line the vertical size of the pupil is measured. Subdividing this line, the left and right edge is detected from each intersection.

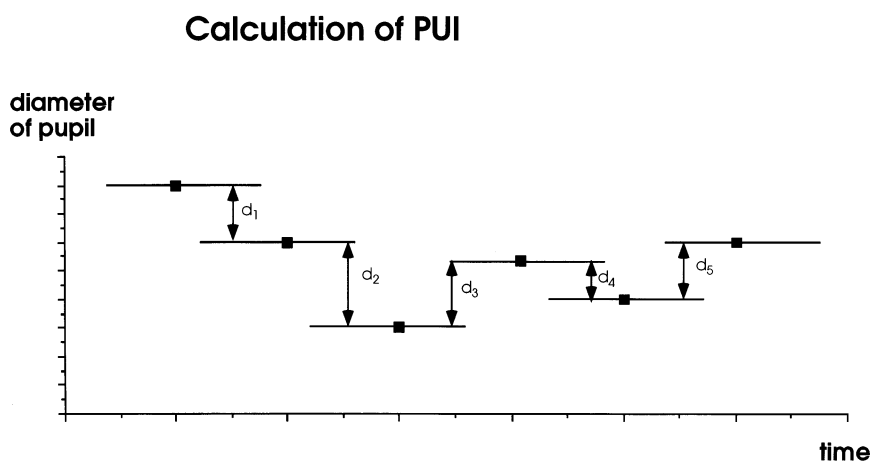


Fig. 3. Calculation of PUI. The absolute differences of averages of 16 data points, are summed up and normalized by time.

most of the following formulas for the 2-D case are similar to those of Groen et al. [3].

$$x_0 = \frac{B_y C_x - B_x C_y}{A_x B_y - A_y B_x}, \qquad y_0 = \frac{A_y C_x - A_x C_y}{B_x A_y - B_y A_x},$$

$$r_0 = \sqrt{\frac{1}{W} \sum_{i=1}^{N} w_i [(x_i - x_0)^2 + (y_i - y_0)^2]}$$

where

$$W = \sum_{i=1}^{N} w_i, \qquad \bar{x} = \frac{1}{W} \sum_{i=1}^{N} w_i x_i, \qquad \bar{y} = \frac{1}{W} \sum_{i=1}^{N} w_i y_i,$$

$$A_x = \sum_{i=1}^{N} w_i (x_i - \bar{x}) x_i, \qquad B_x = \sum_{i=1}^{N} w_i (x_i - \bar{x}) y_i,$$

$$C_x = \frac{1}{2} \sum_{i=1}^{N} w_i (x_i - \bar{x})(x_i^2 + y_i^2),$$

$$A_y = \sum_{i=1}^{N} w_i (y_i - \bar{y}) x_i, \qquad B_y = \sum_{i=1}^{N} w_i (y_i - \bar{y}) y_i,$$

$$C_y = \frac{1}{2} \sum_{i=1}^{N} w_i (y_i - \bar{y})(x_i^2 + y_i^2),$$

The S.D. is calculated additionally:

$$\sigma = \sqrt{\frac{\sum_{i=1}^{N} d_i^2}{N-1}}$$

where d_i is the difference between the radius of the fit and the distance between the centre of the fit and the ith edge point, given by:

$$d_i = \sqrt{(x_i - x_0)^2 + (y_i - y_0)^2} - r_o$$

In the second fit, the weight of the ith data point is

$$w_i = \begin{cases} 1 & for \ |d_i| \leq \max\{\sigma, \sigma_0\} \\ 0 & for \ |d_i| > \max\{\sigma, \sigma_o\} \end{cases}$$

where σ_0 is a certain constant.

If the measurement of the pupil is not very good ($\sigma > \sigma_0$) points with a deviation d_i larger than the S.D. σ are excluded. This method ensures that outliers, e.g. caused by eyelashes, are excluded. In a good measurement, the constant σ_0 ensures that correct points are not excluded (because σ is small in a good measurement even correct points may have a deviation d_i that is larger than σ; thus, they would be excluded without a constant like σ_0). Therefore, in the second fit, only edge points are utilised which are likely to have been measured correctly. The diameter ($= 2r_0$) of the second fit is regarded as an approximation to the pupil diameter.

2.1.4. Quality control of the measurement

As a quality control of the approximation there are

1. the number of data points,
2. the difference between the number of data points on the right side and the left side of the pupil,
3. the S.D. of data points of the second fit,
4. the distance between the centre of the circle and the Purkinje reflex.

These parameters can be used to control the quality of the fit. If these parameters lie in a predetermined interval, the second fit is accepted as the diameter of the pupil.

2.1.5. Vergence and refraction

As mentioned above, horizontal and vertical vergence and the refraction are measured. The vergences can be calculated easily from the horizontal and vertical differences of the centre of the fitted circle and the Purkinje reflex. To measure the refraction, the brightness profile is scanned along the vertical line. Because of the arrangement of the LEDs, the refraction is determined from the slope of the brightness profile. This method is discussed in detail elsewhere [4].

2.2. Data analysis

2.2.1. Artefact rejection

Before off-line analysis, an artefact rejection algorithm is applied to the raw data. In a data segment of

Table 1
Accuracy of pupil measurement of different apertures

Aperture	Mean (mm)	S.D. (mm)	Difference to first aperture (mm)
Whole aperture Purkinje in centre	6.4915	0.0097	—
Whole aperture Purkinje in lower half	6.4175	0.0040	0.074
Upper third of aperture covered Purkinje in centre	6.5072	0.0069	0.0157

ten samples (= 0.4 s) the distance of each data point from the mean value within the segment is calculated and, when exceeding a certain cut-off value, reduced to that value. The procedure is repeated within each ten sample-segment, the next segment always beginning with the second value of the previous one.

The cut-off value may be chosen by the investigator from five predefined values of different strictness. These were obtained from an analysis of 25 normal data sets and means that in 1 (1.11 mm), 5 (0.65 mm), 10 (0.42 mm) or 20% (0.26 mm) of all data segments, an artefact is expected. The fifth predefined value (0.1 mm) was obtained empirically and was found to remove singular events like blinks and high frequency noise quite efficiently without affecting the overall aspect of the data plot.

2.2.2. Fast Fourier transformation

For an off-line analysis of temporal changes in the frequency domain of pupillary oscillation the data set is divided into segments of 2048 samples ($\approx$ 82 s). Missing values are obtained by interpolation. After drift reduction (see below) the mean value is subtracted from each value within the data window. The investigator may desire to apply the Parzen window function (see below) on the data segment, in this case the calculation and subtraction of the mean value is repeated.

Then, a fast Fourier transformation is performed for each data window, using the algorithm published by Press et al. [5]. The results are obtained for each data segment separately in the frequency range from 0 to 0.8 Hz.

One assumption underlying the Fourier transformation is that the signal investigated is periodic. Thus, data sets where the beginning and the end values are not continuous can generate substantially distorted spectra. To manage this effect we use a drift reduction: We calculate a linear regression function for a data segment and subtract it from the data. This results in a satisfying suppression of frequency components leaking in from the lower end of the spectrum.

Table 2
Parameters of the alert and sleepy pupillogram of Fig. 4

	Alert	Sleepy
Diameter of pupil (mm)	7.60	6.77
Power	527	2812
PUI	2.22	10.81

The power spectrum estimate for each data segment (maximum eight segments) is plotted for the frequency region from 0 to 0.8 Hz. In addition, the values of the discrete frequency transforms within frequency bands of 0.1 Hz width (0.0–0.1 Hz, 0.1–0.2 Hz etc.) are summarised, and the contribution of each band to the total 0–0.8 Hz spectrum of the data segment is calculated. The corresponding mean values for the ensemble of all data segments are calculated as well. Incomplete data segments with less than 2048 samples (usually the last segment) are excluded from these calculations.

2.2.3. Changes of the mean pupil diameter

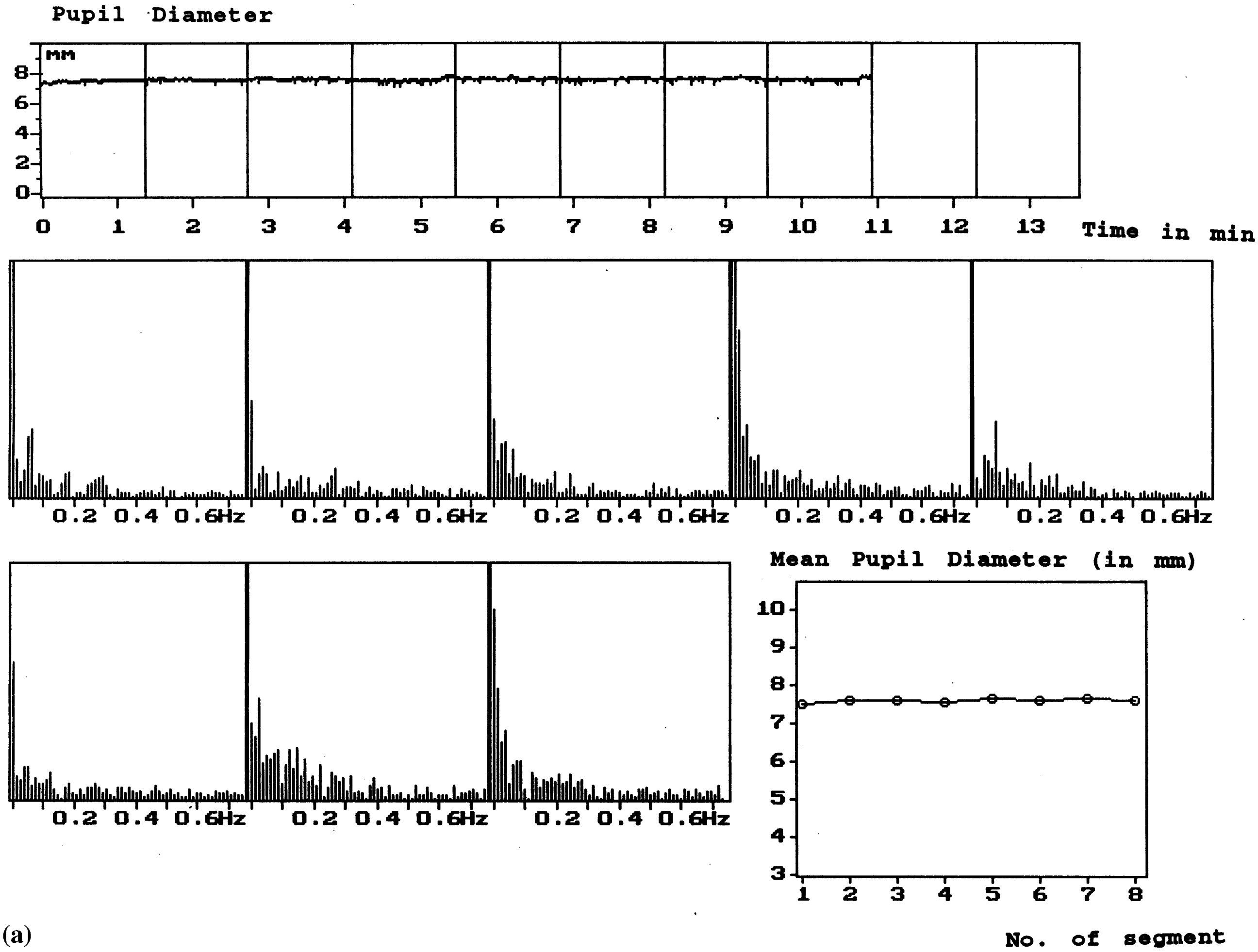
The mean pupil diameter for each data segment (82 s) is calculated after artefact rejection and prior to drift reduction. The values obtained are plotted as a time course of the mean pupil diameter and compared with the overall mean pupil diameter.

2.2.4. The pupillary unrest index (PUI)

In order to obtain a further objective measure for the pupil's tendency to oscillate, we established the pupillary unrest index (PUI) as a numerical parameter. It is based on cumulative changes in pupil diameter. Prior to cumulation, the data are reduced by calculating the average for periods of 16 consecutive values, which serves as a simple low pass filtering and excludes high frequency noise from the following calculation. The absolute values of the differences from one 16-value average to the next one are summarised for each 82 s-data segment (127 differences for one segment). This sum is normalised over a 1 min-period and called the PUI for the corresponding data window (Fig. 3). In addition, the average PUI of all complete data segments is calculated. In short, the PUI is the sum of absolute changes in pupil diameter (in mm) based on a sample frequency of 1.5625 Hz (= 25 Hz/16). Considerations about this parameter were suggested by Loewenfeld (personal communication).

2.3. Pilot study

The pupillary behaviour of 22 healthy men was measured and analysed by the technique described above. The men were devided into two groups according to



(a)

Fig. 4. Pupillograms alert (a), sleepy (b). The two pupillograms recorded in the same subject at two different times. The fatigue waves in the sleepy pupillogram are obvious.

their self-rated sleepiness: ten men (mean $\pm$ S.D.: 48.5 $\pm$ 2.8 years) felt alert, 12 men (46.7 $\pm$ 2.4 years) felt sleepy. The PUI and power in the two groups were compared using the Mann–Whitney U-test.

3. Results

3.1. Accuracy of the measurement

With the described instrumental design, it is possible to detect and analyse about 90 edge points within the 40 ms between successive frames. The accuracy of the method was tested by measuring three artificial pupils. The first and second apertures are circles with the Purkinje reflex in the centre and about half a radius below the centre. To simulate the lid, the upper third of the aperture is covered. All three are placed in such a distance that the images of the artificial pupils correspond to the size of a normal pupil ($\approx$ 6.5 mm). Each aperture was measured 500 times. The results are shown in Table 1. The deviations within each aperture are caused by vibration and thermal noise. Assuming the first aperture is the correct fit, the errors of the two other measurements are less than 0.1 mm (see Table 1).

3.2. Application in volunteers

We demonstrate the results of one subject during sleep deprivation. Because sleepiness increases with the time of sleep deprivation, the hypothesis is that the numerical results of data analysis should increase. Those results are shown in Table 2, the original pupillograms are displayed in Fig. 4.

In the pilot study, there are significant differences in the two groups. The median of the power in the alert group was 721 (mean $\pm$ SD: 711 $\pm$ 195), in the sleepy group 2264 (2458 $\pm$ 1373) the median of the PUI 3.99 (3.76 $\pm$ 1.36) and 7.96 (9.16 $\pm$ 6.13), respectively (Fig. 5). Both differences between the groups were highly significant (power: $U = 0.0$, $P < 0.001$; PUI: $U = 12.0$, $P < 0.001$).

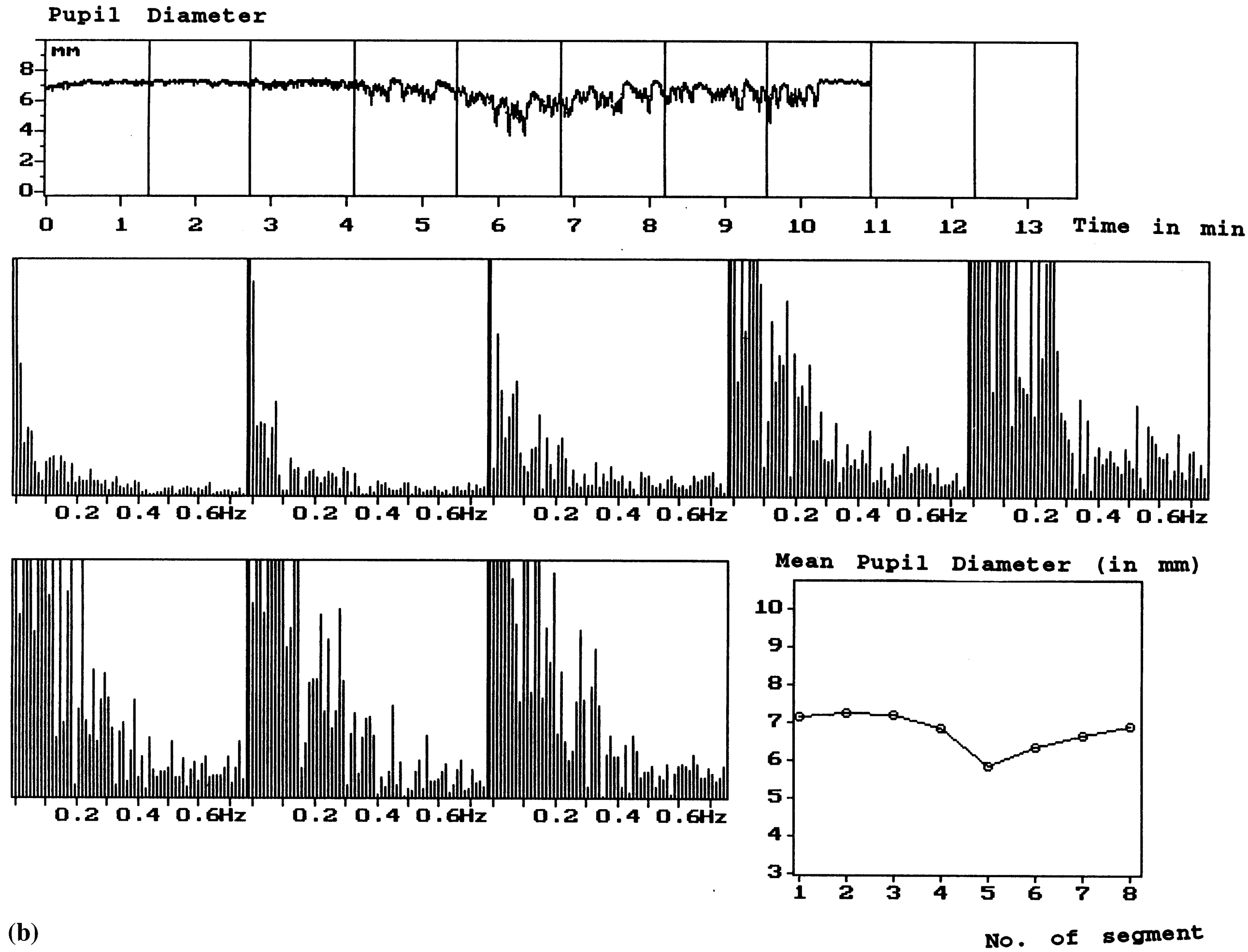


Fig. 4. (*Continued*)

4. Discussion

Pupillography is an important tool both in basic and clinical research. Modern video techniques allow online measurement of the pupillary diameter. Detection of the pupil by means of image processing is usually a minor problem. However, it is worthwhile to have a closer look on how the pupil diameter is measured and calculated. Most of the currently available methods measure the vertical or horizontal diameter directly or they use the pupil area as a parameter.

Our aim was it to design a technique that allows a stable recording of the pupillary size for more than 10 min in a sleepy subject in order to obtain an objective equivalent to sleepiness as suggested by Lowenstein et al. [1] and Lowenfeld [6]. The pupillographic system has to cope mainly with two problems: Droopy eyelids and movement of the eye during the measurement. If only the vertical diameter or pupil is measured, a downward movement of the upper eyelid will simulate a pupil constriction. Theoretically, such artefacts might be eliminated mathematically. However, this is only possible with typical blinks. If the eyelid moves down slowly, the resulting pupillogram might very well look like a fatigue wave. Additionally, horizontal eye movements will also look like fatigue waves. If the horizontal diameter is subject to measurement, vertical eye movements will interfere with pupillary changes.

The only possible method to solve these problems is the application of a mathematical curve fitting procedure to detect the pupillary shape. A method comparable with ours has been developed by Barbur et al. [7]. The system presented here uses a second curve fit in order to eliminate artefacts caused by eyelashes that might erroneously be taken as a pupillary margin. Minor artefacts do not disturb light reflex recordings, because they can be recognised and eliminated on the base of plausibility. This is not the case if the detection of small rhythmic pupillary changes is subject of an investigation. All influences that might simulate spontaneous pupillary constriction or dilation have to be eliminated carefully as far as possible.

It is not possible to avoid blinks completely. Reliable image processing is not possible if only a small part of

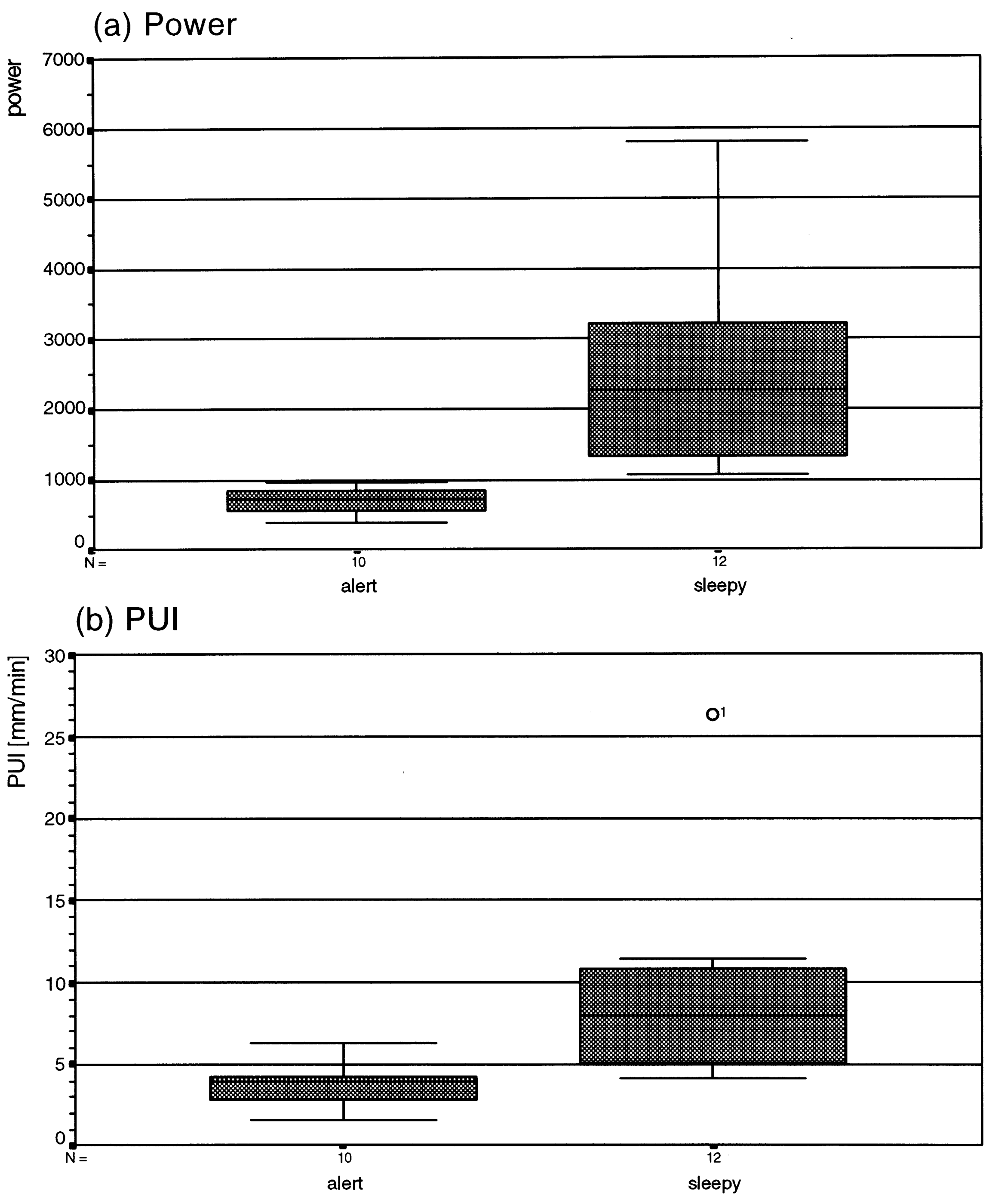


Fig. 5. A box plot is shown for the power (a) and the PUI (b) for the alert and the sleepy group. In the middle the median is shown, the box represent the 25th and 75th percentiles and the lines extend from the box to the highest and lowest values, excluding outliers. Outliers are marked separately.

the pupil is visible. One solution was the application of a lid crutch [8]. However, this is not tolerated very well and influences the level of vigilance. Therefore, we decided to eliminate complete blinks by mathematical methods. Slow downward movements of the upper eyelid and eyelashes do not interfere with our method as long as approximately one half of the pupil is visible (see Fig. 2).

Pupillary changes may also be caused by accommodative changes (near reflex). This in our system is controlled by means of an on-line videoretinoscopy using the brightness profile of the pupil as an indicator of refraction. The disadvantage of this method are problems in patients with high hyperopia or myopia because of a highly inhomogenous fundus reflex. In these it may be necessary to skip retinoscopy and use an illumination that provides an homogeneous light reflex of the entire pupil.

Additionally, we implemented to methods of analysing the pupillograms with the purpose of detecting fatigue waves, i.e. slow pupillary oscillations. One is based on FFT regarding only frequencies below 0.8 Hz, the other is a more illustrative one. It describes the movement of the pupillary margin over time, neglecting fast pupillary changes (> 1.5625 Hz). Further studies with normal subjects and patients have to show which value is superior in discriminating pathologic from normal pupillary behaviour and if the use of the second value enhances the significance of the discrimination.

McLaren et al. [9] introduced numerical parameters to describe slow oscillations of the pupil: Fourier transformation in a bandwidth of 0.02–0.04 Hz and parameters of miosis evaluation. They found a positive correlation between objective parameters of evaluation and subjective assessment of the pupillograms. Although our parameters differ from the parameters they described, there are many similarities, e.g. the FFT in a low frequency band.

The plain differences between an alert and sleepy group of men in power and PUI demonstrate the usefulness of this method to detect and quantify sleepiness objectively.

So far we have introduced a method of pupillary recording over longer time periods that provides stable and reliable values of pupillary diameter and from which pupillary oscillations can be detected and quantified. This method of pupillary measurement is applicable in all settings that require long-time recording of pupil size, e.g. in pupil perimetry [10]. It may be of special interest to apply the method presented in this paper as an objective measure of sleepiness in sleep medicine and sleep research dealing with sleep-disturbed patients or sleepy normals. Additionally, this method may be an appropriate tool in industrial or traffic medicine to check for acute sleepiness in certain professions in order to prevent fatal consequences (e.g. truck drivers, pilots).

Acknowledgements

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