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Pupillometry examinations of the human eye with the eye diagnostic device PEP-2000 – First results

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Abstract: Pupillometry forms the diagnostic basis for numerous pathologies of the eye. For this reason, fast and accurate diagnostics in the field of ophthalmology are essential. Two examination techniques, full-field ERG and pupillometry were combined in a diagnostic device developed by ICM e.V. to reduce the examination process for both examiners and patients. In this paper, the device is examined for the quality of the pupillometry measurements. A study with 12 healthy subjects (3 f, 9 m, 36.33 ± 11.94 years) was conducted to evaluate the device. The results showed that the minimal pupil diameter is 40 % higher than the literature values. The main reason for the differences is the low light intensity of 15 cd/m². However, the maximum pupil diameter is within the range of the researched values. The results of the pupillary reaction measurements show that the values obtained (amplitude, contraction time and peak time) are within the range of literature values. The latency time of 690 ms is 40 % too high. The reason for this could be the moderate pupil detection rate of 50–70 %. Nevertheless, plausible and comparable analysis values could be obtained with the eye diagnostic device PEP-2000. Further work will look at improving pupil detection rates.

Keywords: Pupillometry, Ophthalmology, Human eye, Pupil diameter, Pupillary reaction

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Figure 1: PEP-2000 diagnostic device as stationary and hand-held unit. (Source: ICM e.V.)

1 Introduction

Due to diseases up to blindness of the eye, affected persons lose a large part of their quality of life. The diseases often progress slowly and are diagnosed very late, so the effects have a strong impact on the organism and leave permanent damage, even after the disease has been fought. Some diseases, such as high-pressure glaucoma, are even accompanied by severe pain [1].

For this reason, rapid and meaningful diagnostics are essential in the field of ophthalmology. In most cases, numerous time-consuming individual examinations are necessary before a diagnosis can be made, and the patient can be helped [2]. In order to shorten the examination process for examiners and patients and to reduce costs, the PEP-2000 ophthalmic diagnostic device was developed (see Figure 1). It combines pupillometric and electrophysiological examination techniques in one device setup and can be used stationary as well as mobile [3]. The core of the device is the removable head section, in which a stimulation module is integrated. By means of two LED rings inserted behind the eyecups, flash color, frequency and brightness, as well as background color and brightness can be varied and a wide range of applications can be covered. The acquisition of the pupil images is controlled by a programmable intelligent board camera using two remote head sensors, consisting of each 1/1.8" CMOS, Teledyne e2v greyscale semiconductor. The resolution of the acquired picture of each eye is 1600 x 1200 pixels. The IR sensitive and endocentric optics have very low distortion [3].

In this work, the developed examination device shall be compared with literature values in the field of pupillometry. The evaluation and interpretation of the pupillometry depend on the existence of valid standard or guideline values. It is not possible to rely solely on published data, because the measured parameters are strongly influenced by the device itself and the accessories used [4].

2 Methods

A study design with corresponding subject information and a data protection statement was developed for conducting the feasibility study. Furthermore, the method pupillometry is presented and its evaluation methods and literature values are listed. Finally, the experimental procedure is explained in detail.

2.1 Study design

Suitable subjects were selected by the following exclusion criteria: psychological pre-diseases, recent eye surgeries or ophthalmological pre-diseases, refractive errors above ± 3 dpt, current or previous abuse of addictive substances, neurological diseases, conspicuous reactions (e.g., circulatory collapse, "fainting") to stress-inducing situations, regular intake of medication, allergies/ hypersensitivities of the skin, smoking of nicotine-containing products, and epilepsy.

A two-part data collection form is used to record the key data of the subjects. In the first part of the data collection form, the physical characteristics of the subjects are recorded, and previous diseases are queried in order to detect possible exclusion criteria. In the second part of the data collection form, the subject's current daily condition is queried. The subjects also receive a written information sheet explaining the test procedure, pointing out exclusion criteria and the dangers of the test. From the 25 volunteers, 12 subjects (3 females, 9 males, mean age: 36.33 ± 11.94 years) could be selected for the feasibility study.

2.2 Pupillometry

Pupillometry pursues two central examination purposes: the recording of the pupil diameter as well as the observation of changes in pupil diameter over a defined time interval. The second examination variant can also be referred to as pupillography. In addition, it is possible to view the two pupils of an individual comparatively, for example, to identify disorders of the afferent pupillary pathways [4,5].

In pupillometry, a distinction can be made between the measurement of the maximum and minimum pupil diameter and the measurement of the pupil response to a defined light stimulus. Accordingly, the parameters to be analyzed might differ. When measuring the limit values of the pupil diameter, the pupil is analyzed over a defined period of time and an average value for the minimum and maximum pupil diameter is formed from the measured diameter data in each case. When the response curve is analyzed after a light stimulus, the different time periods of the response play a role in addition to the maximum amplitude [4]. The sequence of the pupil reaction is shown in Figure 2. Table 1 explains these time periods and Table 2 lists typical values of the analysis parameters [4,6,7].

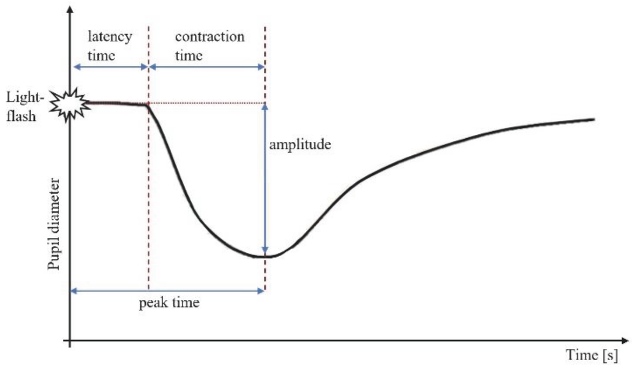

Figure 2: Time progression of the pupillary response to a defined light stimulus, based on [4].

Table 1: Time periods in the pupillary response to a flash of light.

Time periods	Explanation
Latency time	Time between the time of the stimulus and the onset of the pupillary response
Contraction time	Time interval from the onset of pupillary reaction to the time of maximum pupillary contraction
Peak time	Time from stimulus to time of maximum pupil amplitude

Table 2: Analysis parameter in pupillometry [4,6,7].

Analysis parameter	Literatur values
maximum pupil diameter	6.0–8.0 mm
minimum pupil diameter	1.5 mm
Amplitude (Reaction to a light flash)	1.3–1.5 mm
Latency time	140–500 ms
Contraction time	260–700 ms
Peak time (=Latency time + Contraction time)	400–1200 ms

2.3 Execution of experiment

The tests are performed with the PEP-2000 diagnostic device in a darkened room. First, the device position is set for the respective subject. The position of the eyes is checked on the laptop via the real-time display of the device cameras. In the first pupillometry experiment, the maximum and minimum pupil diameters are determined. The subject is dark-adapted for five minutes directly at the device, then the measurement of the maximum pupil diameter is performed simultaneously for both eyes. The value is automatically determined by the device and an average value is obtained. Time periods in which the pupil is not detected are filtered out and not included in the calculation. The eyes are then bright-adapted stepwise until the maximum of 15 cd/m² for two minutes without interruption, after which the pupils are measured again and the minimum diameter is determined [8]. The measurements are performed simultaneously for both eyes. Finally, the pupillary response to a defined light stimulus is measured (pulsed pupillometry). The right and left eyes are stimulated successively with five light flashes at intervals of 5 s and the pupillary response (change in pupil diameter) is recorded as a function of time. The pupil diameter is recorded for both eyes over all ten intervals.

2.4 Data analysis

The pre-processing for pupil detection takes place on the board camera. First, the image is acquired via both image sensors. Simple blob detection is used to search for a prominent reflection in advance, which is then used to determine the image section. In the following, a polar transformation is performed, followed by a contour detection of the pupil shapes. By means of a plausibility check, the found shape is separated from interfering objects. Afterwards, the conversion into metric dimensions is performed by means of an algorithm, which necessarily includes the focusing distance due to the use of endocentric optics. For each subject, the maximum and minimum pupil diameters are measured for the left and right eyes. This results in four analysis parameters for each subject. The four diameter values of each subject are in turn used to calculate the mean value and standard deviation. Mean value and standard deviation are considered separately by eye as well as in general. For the pulsed pupillometry experiment, the procedure is simultaneous. The analysis parameters amplitude, latency time, contraction time and peak time are determined for each subject separately by eye and then mean value and standard deviation, both for both eyes separately and in general, are calculated. The analysis parameters of the individual subjects result from the mean values of the data from the ten measurement intervals of the pulsed pupillometry experiment.

3 Results

The results for the determination of the minimum and maximum pupil diameter are summarized and statistically analyzed in Table 3. Here, "OS" indicates the left patient's eye and "OD" the right patient's eye. The mean maximum diameter of both eyes is 6.46 mm and is within the range of values from the literature [6,7]. The mean minimum diameter of both eyes is 2.08 mm and does not reach the literature value of 1.5 mm [6] and is thus 40 % higher. The main reason for the differences is the lower light intensity, needed to fulfill comparability to other devices or studies [6,8]. Furthermore, it is possible that the system often loses the reference to the pupil when the subject blinks or moves more strongly, which then leads to inaccurate measured values.

Table 3: Statistical values of the analysis parameters of the measurement of the minimum and maximum pupil diameter (PD). (SD- Standard deviation)

Analysis parameter	Mean value	SD
maximum PD - OS	6.28 mm	0.75 mm
maximum PD - OD	6.64 mm	1.01 mm
maximum PD - mean value	**6.46 mm**	**0.80 mm**
minimum PD - OS	1.98 mm	0.37 mm
minimum PD - OD	2.18 mm	0.33 mm
minimum PD - mean value	**2.08 mm**	**0.33 mm**

The evaluation of pulsed pupillometry is summarized and statistically analyzed in Table 4. The comparison of the calculated analysis parameters of the pulsed pupillometry shows that almost all measured values provide comparable results and are within the range of literature values. For the mean diameter amplitude, a value of 1.46 mm was found, which is given in the literature as 1.3–1.5 mm [4]. The mean contraction time of both eyes is 540 ms, comparable values in the range of 260–700 ms can be found in the literature [4,6,7]. Only the mean latency time of both eyes is 690 ms, which is approximately 40 % above the maximum literature value of 500 ms [4,6,7]. This in turn has the consequence that the peak time calculated from this assumes a value of 1210 ms. In the literature, a value range of approximately 400–1200 ms can be found [4,6,7]. The reason for the differences is the average pupil detection rate between 50–70 %. A reduction in the detection rate is caused by a higher process time within the camera controller due to a higher possible artifact occurrence (subject blinks, eyelashes, etc.) and the resulting effort in the plausibility check.

Table 4: Statistical values of the analysis parameters of pulsed pupillometry. (SD- Standard deviation)

Analysis parameter	Mean value	SD
Latency time - OS	690 ms	90 ms
Latency time - OD	700 ms	100 ms
Latency time - mean value	**690 ms**	**70 ms**
Contraction time - OS	540 ms	90 ms
Contraction time - OD	540 ms	120 ms
Contraction time - mean value	**540 ms**	**90 ms**
Peak time - OS	1190 ms	70 ms
Peak time - OD	1220 ms	60 ms
Peak time - mean value	**1210 ms**	**60 ms**
Amplitude - OS	1.19 mm	0.45 mm
Amplitude - OD	1.50 mm	0.34 mm
Amplitude - mean value	**1.46 mm**	**0.38 mm**

A comparison of the averaged analysis parameters between the left (OS) and right eye (OD) shows that lower values were measured in the left eye. In particular, the analysis parameters amplitude, minimum and maximum pupil diameter show difference between 26 %, 10 % and 5 %.

4 Conclusion

In this paper, it could be shown that the developed eye diagnostic device PEP-2000 for pupillometry (determination of minimum and maximum pupil diameter and examination of pupil reaction) provides plausible analysis parameters comparable with the literature. The determined analysis parameters should form the basis for further investigations. However, the quality of the measured values must be improved. By improving the pupil detection rate, a more stable measurement and thus more accurate measurements can be ensured. Further work will address evaluation methods for determining pupil response in pulsed pupillometry. An application of the PEP-2000 in the veterinary field is also currently being investigated.

Author Statement

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