2015 IEEE 28th International Symposium on Computer-Based Medical Systems

Development of an effective method and a portable device to evaluate the pupillary reflex

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Abstract — **Examination of the pupil offers an objective evaluation of visual function as well as the vegetative pathways to the eye. In spite of technological advances and substantial progress in many areas, the routine pupil examination with a conventional light source has undergone no significant changes in the last 100 years. This work proposes the development of an effective and objective method and a portable device to test the direct and consensual pupillary reflex. The first results demonstrate the success of a new device construction and new methodology to record the reflex with differ stimulus, in a situation of complete seal of light.**

Keywords: Pupillary reflex, Consensual Reflex, Pupillography, Pupillometer

I. INTRODUCTION

Examination of the pupil offers an objective evaluation of visual function as well as the vegetative pathways to the eye. Essential information is gathered within a short time. This makes pupillary inspection a valuable part of the ophthalmological, neurological and general medical examinations routine [1].

In spite of technological advances and substantial progress in our understanding of the central nervous system (CNS) pathophysiology, routine pupil examination with a conventional light source has undergone no significant changes in the last 100 years [2]. Pupillary examination involves recording the size, symmetry, and light reactivity of both pupils. Analysis of these parameters is affected by significant interobserver variability due to the influence of factors such as differences in ambient lighting, the examiner's own visual acuity and experience, the intensity of the light stimulus, and the method used to direct that stimulus [2].

Numerous pathologic conditions can disrupt the neural pathways responsible for orbital control or the visual reflex centers and can manifest as a variety of entities, including ophthalmoplegia, oculosympathetic syndrome, Parinaud syndrome, and ptosis [3]. In general medical exams, pupillary examination provides a convenient and simple method for the evaluation of autonomic functions. Most patients with autonomic disorders show evidence of sympathetic or parasympathetic deficits in the pupil [4][5][6].

The parasympathetic system conducts the light reaction with its major center in the dorsal midbrain. The afferent input of the light reflex system in humans is characteristically wired, allowing a detailed analysis of a lesion of the afferent input. To diagnose normal pupillary function, pupils need to be isocoric and react bilaterally equally to light. Anisocoria indicates a problem of the efferent pupillary pathway. Pupillary disorders may involve the afferent pathways (relative afferent pupillary defect) or the efferent pathways. Parasympathetic disorders include dorsal midbrain syndrome, third-nerve palsy, and tonic pupil [7].

In ophthalmology exams, pupil reflex impairment in retinitis pigmentosa [8] and glaucoma [9] may be used to detect occult unilateral or asymmetric maculopathy [10]. A relative afferent pupillary defect (APD), established by the swinging or alternating flashlight test, is an important clinical sign that, when abnormal, is one of the best ways to localize vision loss to the pregeniculate afferent visual pathways (retina, optic nerve, chiasm, and optic tract) [11]. If capable of efficiently recording, detecting, and quantifying relative afferent pupillary defects, a portable pupilometer could be used to screen patients with vision loss [11].

Studies have shown that pupil reflex impairment in patients with Parkinson's disease without overt autonomic dysfunction [2][12][13].

The cranial nerve III is closely linked to the medial part of the temporal lobe (uncus of the hippocampus) and to areas of the brainstem, which control consciousness. Therefore, any lesion or hypoperfusion in the midbrain or in the efferent fibres forming the cranial nerve III causes pupil dilation, which is usually ipsilateral to the lesion [2][14][15][16]. Early detection could therefore be associated with better clinical progress and facilitates starting treatment [2][17].

Over the last few years, infrared devices included in digital cameras have led to the development of digital systems, which enable outside researchers to carry out repeatable non-invasive studies of pupil size and light

2372-9198/15 $3.00 © 2015 IEEE
DOI 10.1109/CBMS.2015.41

reactivity using an objective method [2][11][18][19][20]. However, it is not a portable device capable of testing direct and consensual pupillary reflex.

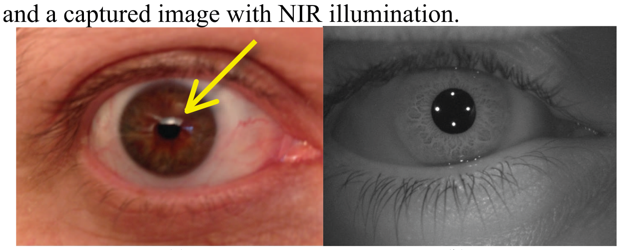
The purpose of this work is the development of an effective and objective method and a portable device to test the consensual pupillary reflex. This method can improve the prediction of neurological and ophthalmological deterioration of the patients, avoiding unnecessary tests and allowing early therapeutic intervention.

II. ANATOMY OF THE HUMAN OCULAR SYSTEM

A major challenge when working with human eye images is the correct technique for image capture. This task is not trivial, mostly because the visible structure of the human eye, composed of sclera and iris, reflect visible light exceptionally well. These reflections form white spots that overlap images, preventing correct measurements of contraction and pupil dilation movement.

Moreover, research in the biometrics area has proposed equipment with special Near Infra-Red (NIR) lighting to capture human eye images [17][18][19][20][21]. This type of lighting is not visible to the human eye and thus does not offer visual stimulus for the pupil to execute its miosis and mydriasis movements.

The human optic nerve carries the afferent visual signals captured through the eyes to the Edinger-Westphal nucleus region, whose axons are directed to the right and left oculomotors. Thus, any inadvertent movements performed by an eye are reproduced in the other eye [22][23][24]. Fig. 1 shows an example of a captured image with natural lighting and a captured image with NIR illumination.



(a) (b)

Figure 1: Difference between common light (a) and NIR light (b) light to capture images from human eye.

III. MATERIAL AND METHODS

A. Pupillometer construction

A pupillometer was built based on consensual human optics reflection. The pupillometer has a lighting system with visible light that gradually goes from 0 (zero) to 38 lux, positioned at 3 centimeters distance from one of the eyes.

While the lighting system provides stimuli for pupil response, a set of four infrared LEDs provide invisible light to the human eye, allowing the camera to record images. These LEDs operate on an 850 nm wavelength, not providing stimulus for pupil contraction and dilation. The camera that records the images is a Point Grey Firefly MV 0.3 MP Mono USB 2.0 (Microm MTV022). Fig. 2 shows a picture of a pupillometer being used by a volunteer.

Figure 2: Volunteer using pupillometer.

B. Construction of a video database

The built pupillometer has a circuit that is controlled by software developed in C++ that allows setting parameters to record. We selected 20 volunteers with no pre-existing disease, either ocular or systemic. Each healthy volunteer was placed in a dark testing room for approximately 5 minutes, to adapt to darkness. Before the recording started, the volunteer was asked not to blink.

Experiments were performed with the recording of 50 seconds videos, at a recording rate of 60 frames per second. At every 10 seconds, a 1 lux visual stimulus was applied for 10 seconds. Therefore, in each video recorded, were registered three intervals without visual stimulus and two intervals with visual stimulus. The adopted visual stimulus methodology is shown in Table I.

Each visual stimulus time was set to ensure the complete capture of the pupil contraction or dilation movement with a safety margin. Intensity of visual stimulus 1 lux is sufficient to stimulate the pupil to a full contraction without causing discomfort to the person being filmed. Unlike other studies in the literature [25], the white light source is positioned 3 centimeters away from the stimulated eye and any external lighting was completely sealed, as shown in Fig. 2.

TABLE I. VISUAL STIMULUS SPECIFICATIONS

Frames	Visual Stimulus
1 – 600	OFF
601 – 1200	ON
1201 – 1800	OFF
1801 – 2400	ON
2401 – 3000	OFF

This methodology was applied in both eyes. In one video, was applied stimulus light and recording the same eye. Afterwards, in other video, with the stimulus light in an eye and recording the other eye, to test a consensual reflex.

In order to evaluate results, six metrics similar to the tests performed by Chang et al. [25] were applied. They used visual stimuli ranging from 0.6 to 2.1 seconds long. The volunteer was not in a sealed lighting environment, but in a room with partial lighting, so the applied visual stimuli ranged from 25 lux in the dark, to stimulate pupil dilation, to 35 lux in the clearest stimulus, to stimulate pupil contraction.

The constructed pupillometer in this work completely seals illumination, as seen in Fig. 2, and visual stimuli were of 0 lux to stimulate a full mydriasis and 1 lux to stimulate a maximum miosis, without discomfort for the volunteer. The six measures used for testing were. The six metrics used to test methodology were:

- Maximum Mydriasis - demonstrates the largest pupil diameter before contraction.
- Maximum Miosis - demonstrates the smallest pupil diameter afterwards contracting.
- Amplitude (Amp) - shows in percentage how much the pupil constricts afterwards applying 1 lux visual stimulus.
- Latency (Lat) - shows the time in seconds that the pupil takes to start contraction afterwards visual stimulus application.
- Time to maximum contraction (TMC) - demonstrates at what time in the 10 seconds stimulus the pupil reaches its maximum contraction.
- Time to maximum dilation (TMD) - demonstrates at what time in the 10 seconds of light stimulation absence the pupil reaches maximum dilation.

The variables analyzed included maximum mydriasis, maximum miosis, amplitude, latency, time to maximum contraction and time to maximum dilation. The authorization to carry out this footage was submitted and approved by the Ethics Committee in Research (CEP), in a submitted project in Plataforma Brasil, under the number CAAE 23723213.0.0000.5083.

IV. Results

In some cases, the volunteer movements caused failures in targeting the pupil and therefore, caused noise in the signal. In these cases, the signal was filtered by the neighborhood average algorithm.

160 videos were carried out, with 6 to 12 videos for the 20 volunteers. 5 volunteers were females (25%) and 15 males (75%). The average age was of 29.0 ± 8.2 years. All videos were normalized by Z-Score.

Table II and table III shows the average values and its standard deviations for all videos of the volunteers. The 1st period corresponds to frames 601 – 1800 and 2nd period corresponds to frames 1801 – 2400 when the light is switch on.

The table II presents values of the right eye filmed. The stimulus light is applied in the filmed eye.

TABLE II. Direct response

	1st Period		2nd Period	
	Mean	**SD[a]**	**Mean**	**SD[a]**
Mydriasis	1.61	0.47	1.64	0.56
Miosis	0.02	0.02	0.02	0.05
Amp	1.34%	-	1.40%	-
Lat	0.54 seg	0.13 seg	0.49 seg	0.15 seg
TMC	0.20 seg	0.10 seg	0.23 seg	0.44 seg
TMD	3.59 seg	0.51 seg	3.35 seg	0.73 seg

a. Standard Deviation

The table III presents values of the right eye filmed. The stimulus light is applied in the left eye.

TABLE III. Consensual response

	1st Period		2nd Period	
	Mean	**SD[a]**	**Mean**	**SD[a]**
Mydriasis	1.44	0.25	1.41	0.39
Miosis	0.02	0.03	0.01	0.04
Amp	1.14%	-	1.15%	-
Lat	0.47 seg	0.15 seg	0.45 seg	0.28 seg
TMC	0.17 seg	0.04 seg	0.17 seg	0.05 seg
TMD	3.56 seg	0.65 seg	3.69 seg	0.60 seg

a. Standard Deviation

Some differences between the response distributions to reflex pupil noted. The miosis on consensual reflex was bigger than direct reflex. The mydriasis, amplitude, latency and TMC on consensual reflex was samaller than direct reflex. The TMD ranged according to study period.

Fig. 5 show that the pupil were symmetric when the study began. Moreover, the pupils were asymmetric afterwards light stimuli and remains throughout the study.

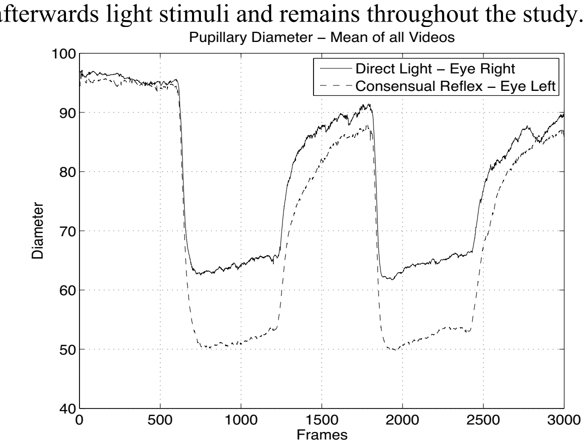


Figure 5: Pupillary diameter between frames 950 and 2050.

V. Discussion

Pupillography has been used to characterize further the features of the swinging flashlight test, but it has not become a tool that is used in ophthalmic practice to identify or observe patients with neurogenic vision loss [26].

The pupillometer constructed proved to be an effective, non-invasive, objective, and portable pupillary change identification method based on light stimulus.. Images captured were carried out efficiently, without the need to repeat examination by measurement error. In some cases, the volunteer movements caused failures on pupil segmentation and, therefore, caused noise in the signal. To correct them, the software used the neighborhood average algorithm. The built pupillometer completely seals lighting, and visual stimuli were of 0 lux to stimulate the pupil to full dilation, and 1 lux to stimulate the pupil to a maximum contraction, without discomfort to the individual.

The tests showed a pupil diameter difference between the direct light reflex and the consensual light reflex. This little difference between the reflex shows the importance and need for a computerized method, so it is not possible to detect on clinical practice. The difference between a right reflex and consensual reflex named relative afferent pupillary defect is presented by a 0.3 log of world population [26][27]. Nicholas J. Volpe found that them volunteers with simulated APDs were similar to patients with APDs resulting from optic neuropathies. The magnitude of intereye differences with different levels of APDs for each parameter was the same regardless of whether it was a simulated APD or a true APD.

The pupil were symmetric afterwards adapt to darkness, moreover, the pupil were asymmetric afterwards light stimuli and remains throughout the study. Showing that the optical path afferent and efferent has properties depolarization and repolarization of the two routes. So we need more studies to interprets and standardize these features.

VI. Conclusion

The pupillometer allowed the evaluation of size, symmetry, and light reactivity of pupils. Test interference factors were eliminated such as: ambient lighting, observer experience, light stimulus intensity, and the method used to direct this stimulation. The pupillometer proved to be an effective, non-invasive, objective, and portable pupillary reflex test method based on light stimulus.

This work can also open a way to new studies involving computer-aided diagnosis (CAD). Changes in the software could possibility enable studies to identify signals of a probable disease. Therefore, further research is warranted to standardize dark adaptation time before the start of the test, the light intensity, duration of the light stimulus, and the interval between them.

Acknowledgment

Thanks to the Foundation for Research Support of the State of Goiás (FAPEG), which provided financial resources for the development of this research. Thanks to the National Research Council (CNPq) for providing conditions for the development of this research. Finally, thanks for all the volunteers who contributed to the success of this research.

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