Techniques and Equipment for Automated Pupillometry and its Application to Aid in the Diagnosis of Diseases: A Literature Review

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***Abstract*—This work aims to investigate, by means of a Systematic Literature Review, to evaluate the current state of the use of artificial intelligence in automated pupillometric technology and its application in helping to diagnose diseases, to identify the methods and equipment used and propose case new equipment based on computer vision is feasible. We also investigated the accuracy of methodologies and equipment that use computerized pupilometry to identify pathologies or disorders, as well as the viability and usability of existing pupilometers. In this sense, creating a pupilometer capable of stimulating and varying wavelengths, providing an interface to preview the exam, and embedding the classification algorithms is a great challenge. In this systematic review of the literature, we consider publications from the last ten years (2010 - 2020) indexed by seven solid scientific databases. The review identified a vast amount of work on pupillometry; however, a small amount related to the construction and viability of a pupilometer with an embedded system, easy to use and with a preview interface. Having identified this, we propose a new methodology for the construction of the pupilometer as well as the algorithm for extracting the characteristics through pupilometry.**

***Index Terms*—Artificial Intelligence, Diagnosis, Pupilometry, Low Cost**

I. Introduction

As all diseases have a cause and act by certain mechanisms, which produce morphological and / or molecular changes in tissues, which result in functional changes in the organism or part of it, producing subjective (symptoms) or objective (signs) changes [1]. These changes are identified through exams, such as medical imaging exams. Based on these tests, doctors perform the diagnosis and assess the clinical status of patients. The current difficulty in identifying pathologies through a single exam and coupled with the self-cost of these procedures, make it difficult to diagnose diseases, which, if treated early, the patient's health condition can be reversed.

Being able to make the diagnosis through precise metrics, in a fast, safe, efficient way, with non-evasive means and at a low cost, brings great advantages, which if done in the first days allow an adequate treatment for the disease from the beginning. In the field of neurology, pupillary responses are a simple metric and need to assess the neurological activity of the patient in which it is used to verify brain death. There is an intrinsic relationship between the pupillary reflex and the central nervous system, in this sense the analysis of pupillary behavior combined with the use of computer vision technologies has shown good results for the early diagnosis of neurological diseases [2], and there are currently several studies that use the analysis of pupillary behavior to aid in the diagnosis of several diseases, not only those related to the central nervous system.

In this RSL we deal with the point of view of the feasibility of diagnosing pathologies through automated pupillometry and the feasibility of a pupilometer capable of stimulating at various wavelengths, with an interface for exam preview, with algorithms to extract the characteristics of the pupil behavior and that has a low cost of construction and implementation.

II. Work Development

For the development of this work, a selection plan of the keywords, research questions, quality criteria of the works and choices of the databases were made. Subsequently, the work was conducted in a preliminary manner through the reading of the titles and abstracts, after which in more depth the complete reading of the works selected in the preliminary phase and quality classification was done.

A. Research Methodology

For this work, a study was carried out carrying out a Systematic Literature Review (RSL) in seven scientific databases, because when doing the SRL, relevant studies about the question raised are gathered. With this, there are well-defined bases for the identification, evaluation, synthesis and interpretation of the relevant evidence for a given research question. Following the RSL guideline defined by [3] three main steps were taken: (i) Planning; (II) Conduction; and (III) Summary of the data. In the first stage it was defined: (I.1) Research objectives; (I.2)

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Research questions; (I.3) Keywords, synonyms, inclusion and exclusion criteria for study selection; and (I.4) a checklist for evaluating the quality of the study. In the second stage the steps were done: (II.1) Literature search in selected databases; (II.2) Selection of the most relevant literature study; (II.3) Literature quality assessment. In the third and last part is this work in which the theme and research problems are synthesized.

B. Research Objectives

Our research group has been working for a few years with the analysis of pupillary behavior, and some difficulties related to the capture equipment, the pathology in which the existing equipment is able to identify and the use of the equipment by ophthalmologists have been identified. To analyze if there is already any equipment that helps in these difficulties, we carried out a systematic review of the literature, in which the main objective is to answer the following question: "It is feasible to build a low cost automated pupilometer capable of stimulating at various wavelengths with a simple and friendly interface for researchers in the field of health and that has the possibility to assist in the diagnosis of any pathology for which it was programmed? ". To answer this great question, we subdivided the research questions into more specific questions: (QP.1) What are the methods for identifying the pupil? (QP.2) Sensors used? (QP.3) Characteristics extracted by the method? (QP.4) Help in the diagnosis of more than one disease? (QP.5) What are the methods for diagnosis ?.

C. Keywords, synonyms and search strategy

The keywords chosen for conducting RSL are words that are directly related to the theme of RSL, in addition to describing the problem in question well. At the same time, we chose synonyms associated with each key word, all words and synonyms being in the English language because it is the most used language in the scientific world: (K.1) Automated (Smart); (K.2) Intelligence (Intelligent); (K.3) Pathology (Anomaly, Disease,Disorder); (K.4) Pupillometry (Pupil Detection, Pupillary, Pupillometer, Pupilometer, Pupil response). The general logic search string was defined as: (Pupillometry OR Pupil Detection OR Pupillary OR Pupillometer OR Pupilometer OR Pupil response) AND (Automated OR Smart) AND (Intelligence OR Intelligent) AND (Pathology OR Anomaly OR Disease OR Disorder). This string has been adjusted for each electronic database to meet its search syntax. We searched seven databases: (1) ACM Digital Library; (2) El Compendex; (3) IEEE Digital Library; (4) ISI Web of Science; (5) PubMed; (6) Science Direct; (7) Springer Link; since they gather the majority of publications in the field of medicine and applied computing in medicine. In order to concentrate the search on the most relevant articles, the search was made only on articles in the English language and the search chain was applied only to the titles, keywords and abstracts of the databases. This narrowed down the search to have a number of manageable results.

D. Inclusion / Exclusion criteria

Inclusion and exclusion criteria were defined using a cut-off score. This score is obtained through a quality assessment list, which aims to restrict studies on related and quality work for RSL. The quality assessment list was defined on three issues: (AQ.1) Do you use low cost equipment?; (AQ.2) Does it aid in the diagnosis of any disease?; (AQ.3) Efficient Algorithm?; (AQ.4) Method with good results?; (AQ.5) Demonstrate the technique used clearly?. Since for each quality assessment there are three possible answers: I'm not sure, Yes and No. A weight was assigned to each answer and the answer I am not sure the weight is 0.5 the answer Yes has weight 1 and the answer No weight 0. With the weight assigned to each answer, the works that were selected are the ones that will add 3 points in the quality assessment.

E. Conducting the review

With all the planning part previously described, with the research conditions corrected, the databases were applied. Subsequently, in the study selection stage, the bibliographic references were evaluated according to the inclusion and exclusion criteria. In some cases the full text was consulted, as only with the title and abstract did not have a specific idea of the work. A Table I it shows the number of papers retrieved when searching in each database and the number of studies accepted (selected) and rejected during the selection stage. In total, only 60 studies were accepted. In the preliminary phase it was possible to discard most unrelated works. Finally, all accepted articles were read in full.

TABLE I
NUMBER OF PAPERS (2010 - 2020) IN RSL

Data base	Total	Duplicates	Accepted	Rejected
ACM Digital Library	141	0	0	141
El Compendex	7	1	1	5
IEEE Digital Library	31	0	21	10
ISI Web of Science	1	0	0	1
PubMed	29	1	8	20
Science Direct	165	7	20	138
Springer Link	312	7	10	295

III. LITERATURE REVIEW

In this section we provide an overview of the pupilometers used in the selected works in RSL, techniques used to extract information on pupillary behavior and the methods used for diagnosing pathologies.

A. Capture Equipment

All works bring in their demonstration capture equipment assembled with the most diverse artifacts, from glasses with webcam printed in 3D prints to equipment that are already used by neurologists with the EeurOptics PLR-200. We also identified that in most works the equipment is built with the specific objective of tracking the look. In these cases the cameras are positioned in front of the person at an average distance of 70 centimeters in which the main objective is to identify where the person is looking and in some cases the pupil behavior when the person visualizes a target. For the specific study of pupillary behavior in order to assist in the diagnosis of some pathology, this type of camera arrangement does not offer good accuracy. In some cases, such as [4] and [5] the objective is to analyze pupillary behavior, however the camera is distant or outside the central axis in which the pupil can be seen from the front. In previous works in our research group as in [6] we identified that any type of light that falls on the pupil interferes with its diameter. Therefore, in the methods which the camera is away from or which allows the incidence of light in the pupil, it offers good accuracy for medical examinations. In this sense, the work that involves eye tracking that has been of great value in the field of the pupil identification algorithm through images because the equipment and the shape that are designed are not useful for the purpose of this RSL. We also identified that the works with the best results are those that use near infrared cameras, as they give greater control over the lighting and allow the pupil to be visualized with low visible illumination.

In studies in which the equipment is specific for the analysis of human pupillary behavior, we identified that several studies used the same equipment because it is a device widely used in clinics and hospitals by neurologists, such as the EeurOptics PLR-200. However, this equipment has a high cost and the software embedded in it is specific to identify neurological problems.

Another relevant point that was analyzed is the equipment's ability to perform stimuli at various wavelengths. As demonstrated in the work of [7] who is the partner ophthalmologist in our research group. In which it demonstrates the advantage of being able to make stimuli in several wavelengths.

B. Capture and stimulus method

In the analysis to identify the capture and stimulus methods we can see that in most cases only two LEDs (light emitting diodes) are used, one near infrared and the other being red, green or blue. In the work of [8], a near infrared and a light red LED were used, making the equipment useful only for analysis of pathologies so that the pupil is more reactive to red light.

In the work of [9] three types of LEDs are already used, near infrared, red and green. Com are controlled separately by a microcontroller and the cameras are fitted using supports printed by 3D printers on conventional glasses.

Another important point that we analyzed because we had a problem is the usability of all the equipment. For the main objective of the research group is to create a product and method to aid in the diagnosis of diseases or disorders minimally viable, so that it can be used by researchers from all over the world. With this we can identify that in the work done by [8] the equipment that performs the stimulus is disconnected from the recording camera and does not have easy to install and use software. The work of [10] shows a more robust equipment that is capable of stimulating in various colors and has a low construction cost. However, it does not have protection against ambient light and software that is easy to install and use.

C. Pupil Detection

Pupil detection is a known problem in computer vision and is basically treated as a problem of detecting circles in an image. Particularly the images of the human eye have been widely explored for various applications such as cocular tracking. In this sense, [11], it demonstrates that a real-time eye tracking system is important for many Human Computer Interface applications, including stereoscopic synthesis, extraction of information from the person's attention, behavior analysis, etc. To make a real-time eye tracking system feasible, the system must have an efficient pupil detection algorithm and environment-independent image processing, in addition to a small and low complexity capture equipment. In the phase of detection of the pupil in the images collected by the equipment, the algorithms are similar to those of tracking the gaze, the detection parts of the face and the direction of the gaze.

Another approach that uses a lot of human eye images is biometric identification through the iris. In this approach, the iris and its border with the sclera are identified, the pupil and its border with the iris are also identified. In this case we would have two circles inside each other, one being the iris and the other being the pupil.

In the digital processing of the images of the human eye we have among several problems the problem of the reflection of light in the eyes. Such a reflex can be very harmful and hide various information. In this respect, [12] proposes a pupil detection method in which it is robust and immune to reflexes. Later in this work, we will approach this method.

In the method demonstrated in the work of [13] the entry for the algorithm is a grayscale image. In the first step, the color histogram is analyzed and the algorithm decides whether it expects the pupil to be bright or dark. For bright pupils, the algorithm selects the curved edge with the darkest closed intensity value. This is done by refining the filtered image result with morphological operations to enhance the border. The remaining edges are analyzed if they are curved or straight. For curved edges, the eclosed inactivity value is calculated and the best one is selected.

Basically the circle detection algorithms follow the following steps: Image smoothing, by smoothing filters to reduce noise, one of the most used filters is the Gaussian filter, then the image is binarized and later the edge detection is done . Finally, a circumference descriptor or a circumference identification method is used.

The most consolidated method for identifying circumference is the hough transform in which it makes use of an accumulator matrix in a parameter space. The method is very efficient for detecting lines and circles even if they have gaps, but it has a high computational cost. Another way to identify is through a descriptor that models a circle. And there are still some processes that help in the detection, which is the use of mathematical morphology, since the environment, the lighting are controlled and we know the format we are looking for.

Another approach is the use of convolutional neural networks, as shown in the work of [14], which in a user study with eleven participants, comparisons show that PupilNet which is a methodology using CNNs outperforms other algorithms in measuring pupil dilation, is robust for various lighting conditions and robust for different eye colors. However, this technique has a computational auto cost.

IV. Conclusion

This RSL highlights studies that demonstrate consistent results in which the identification of the pupil is made accurately through images of the human eye. It also shows that the aid in the diagnosis of diseases or disorders through human pupillary behavior is a promising technique. It also highlights that works that aim at the identification of the pupil and its behavior serve as bases for works in which they approach more deeply the intelligence in the interpretation of the data extracted by identification methods.

Carefully controlled conditions are necessary to avoid reflection and to extract the metrics for clinical screening. With this we have a great way to improve the diagnosis of some pathologies or at least point to which more robust clinical examination the patient should be forwarded to. However, robust findings are still limited as to the effective diagnosis of the pathology or whether the method demonstrates specificity to identify the pathology in relation to other symptoms. In order to improve this aspect, more in-depth research on the subject and a larger sample of exams is needed.

Based on this RSL, we found that, in recent years, there have been significant advances in the diagnosis of pathologies through pupillometry. However, few studies deal with the effective usability of diagnostic methods and the viability of the pupillometer. Most studies focus on extracting data from pupillary behavior, with little or no attention to the viability of the diagnosis by these methods. Another aspect that is not much discussed is the general use of the equipment.

With this, this systematic review of the literature shows that the construction of an equipment for the analysis of pupil behavior capable of stimulating at various wavelengths, capable of blocking the incidence of external light in the pupil, coupled with an intuitive system of easy installation and usability, configurable for the identification of various pathologies together with an artificial intelligence system for training and learning for new diseases or disorders, it becomes a great ally in research related to human pupillary behavior.

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