Novel Chromatic Pupillometer: Portable Pupillometry Diagnostic System

Peyton Paulick[1], Philipp Novotny[2], Mark Bachman[1], and Herbert Plischke[2]

[1] Department of Biomedical Engineering, University of California Irvine, 2227 Engineering Gateway, Irvine, CA 92697, USA
[2] Generation Research Program der Ludwig-Maximilians Universität München, Prof. Max Lange Platz 11, 83646 Bad Tölz, Germany

Abstract. This research study explores development of a novel chromatic pupillometer that can analyze the characteristics of a patient's pupil light reflex (PLR). Characteristics of the PLR are not only used to determine retinal function but also have been recently used as a non-invasive diagnostic for a variety of neurological disorders and diseased states. This device is a compact diagnostic goggle that contains both stimulating and recording abilities of the PLR. This paper will discuss the design and function of the prototype as well as present preliminary data on evaluation of a subset of cells within the PLR.

Keywords: chromatic pupillometry, pupil light reflex, ipRGCs, pupillometry, eye tracking, assistive device, portable system.

1 Introduction

The pupil light reflex (PLC) has been of great interest to physicians and scientists alike not only for its ability to represent retinal function, but to serve as a marker for other diseased states [1–5][1], [3], [5]. Researchers are now exploring the pupil light reflex as a diagnostic measure for retinispigmentosa[4], Parkinson's and Alzheimer's disease [6], [7] , optic neuritis [8], diabetic autonomic neuropathy [9], head injury [10], and many others. This thus makes the pupil light response compelling to study and utilized as a non-invasive clinical measure of a variety of diseased states. More recently the importance of the pupil response to specific wavelengths at ranging intensities has been described as a protocol to asses inner and outer retinal function [1], [4], [11]. Due to the recent nature of these studies a combined pupillometry system has yet to become commercially available. Most systems are composed of a light stimulating system and a separate eye tracking system, none of which are portable. Our group is interested in creating one combined non-obtrusive system that is portable and easy-to-wear. This paper will discuss our novel non-obtrusive chromatic pupillometer and some preliminary data evaluating one specific cell population of the PLC: melanopsin-expressing intrinsic photosensitive retinal ganglion cells(ipRGCs).

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2 Materials and Methods

The objective for the CPG was to create an all-in-one device to simultaneously stimulate and record the pupil light reflex. The left eye will be illuminated by a stimulating sphere composed of LEDs and the right eye will contain the eye tracking unit to record the pupillary light reflex in response to stimulation. The response of both pupils in normal conditions is identical, regardless of which eye is being exposed to stimulation [15].

The frame of the chromatic pupillometry goggles (CPG) was made from an off the shelf pair of welding goggles with removable eyepiece and an elastic head strap. This pair of goggles is relatively lightweight and comfortable to wear. Each eye frame was fitted with a magnet embedded acrylic ring. Both the stimulating and recording units of the CPG have a magnetic ring base; therefore can be easily connected to the frame of the goggles. This design feature allows for easy transport of the CPG and for components to be interchangeable. Test subjects place the goggles onto the head then both stimulating and recording units can be clipped into place using the magnetic attachment feature.

Fig. 1. A standard pair of welding goggles with removable housing and eyepiece was used as the foundation for the chromatic pupillometry goggles (CPG). Each eye socket was outfitted with anpolystyrene ring embedded with magnets to allow both the stimulating light sphere and the pupil recording components to click on to the eye in a 'plug and play' method.

2.1 Light Stimulator

The light-stimulating unit of the CPG is made of a hollow plastic sphere with an interior coating of titanium dioxide white paint for increased reflectance [16]. Six RGB (Red, Green, Blue) LEDs are mounted on the magnetic polystyrene ring at a 45° angle and sealed within the hemisphere. This design configuration allows for increased uniformity of light dispersion within the sphere. The stimulating sphere is assembled with a connector that will connect the stimulating sphere the RGB controller. As demonstrated in Fig.2c the sphere is easily removed and attached to the frame of the CPG goggles.

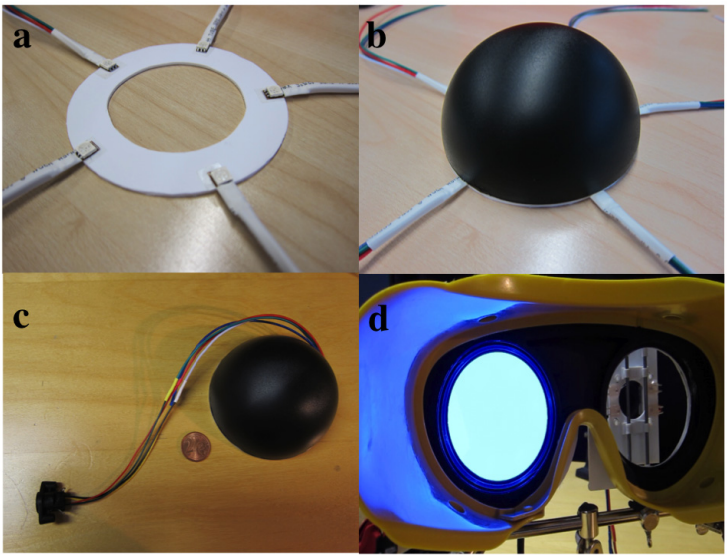

Fig. 2. The CPG light stimulating sphere a) demonstrates the acrylic ring embedded with magnets and the RGB LEDs mounted radially along the ring at a 45°b) the RGB LED array sealed within the hemisphere c) Completed RGB stimulating hemisphere attached with a connector to power and control the LED array d) stimulator fully assembled and attached to the goggle frame. This demonstration is showing a 100 cd/m^2 blue light stimulation.

In order to control the output of the stimulating sphere to create a specific lighting scheme of interest we will use a RGB (Red-Green-Blue) microcontroller that will execute the lighting sequence. The RGB controller used in this prototype is a 'MS-35' (CONRAD GmbH; Munich, Germany) and is featured in Fig.3. This controller comes with an easy to use graphical user interface (GUI) to send several settings and sequences to the unit via the USB programming cable. Once a specific sequence is set it can be saved to the controller's memory and the USB connection is no longer required. The controller is 8-bit controller thus allows for 256 step setting for the diming/brightness of the LEDs. All three of the colors are controlled independently. The driving voltage for both the microcontroller and the LEDs is 9V DC.

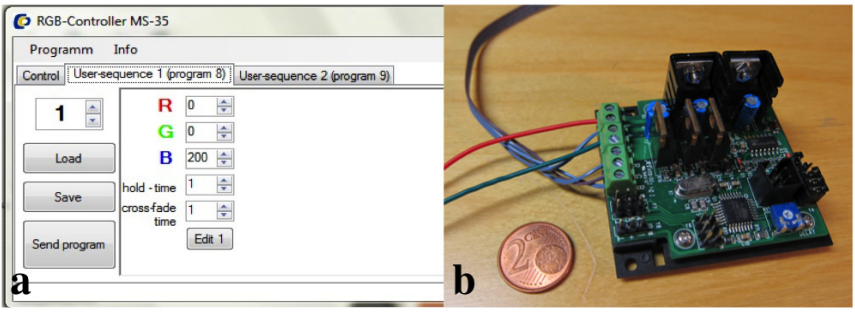

Fig. 3. a) Figure demonstrating the Conrad MS-35 RGB microcontroller interface. Specific protocols can be imported into the user sequence and the intensity of the light controlled by the inputted value. Duration is controlled by the hold-time feature, then a program is sent directly to the microcontroller and subsequently to the light stimulating unit b) Figure of the actual RGB controller with connections for power, ground, and RGB LEDs.

In order to convert the value used in the microcontroller GUI into a photometric measure a calibration of the light emitted from the stimulating sphere must be performed. A spectroradiometer (JETITechnischeInstrumente GmbH; Jena, Germany) was used to characterize the visible range of spectrum produced by our stimulating sphere when driven by a 9V power source. The spectroradiometer was placed approximately 1" from the base of the stimulating sphere, which is the distance the eye will be from the stimulating sphere during testing. The characterization reports values of luminance (cd/m2), radiance (W/sr*m2), dominant wavelength, and color purity. This calibration was repeated at three microcontroller step values, 50, 100, 200) and their results compiled to generate a conversion factor that can translate the 0-255 step value of the microcontroller to photometric measures of luminance and radiance for each color.

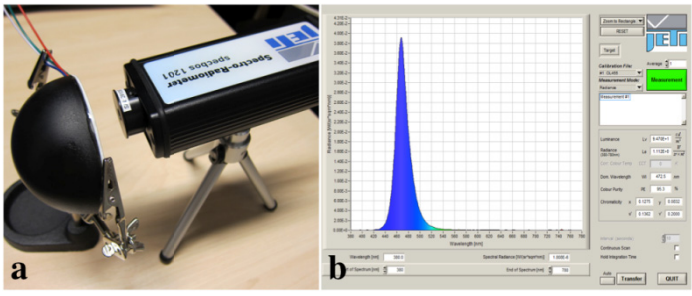

Fig. 4. a) Spectrometer testing setup for evaluation of the different lighting scenarios of the stimulating sphere b) spectrometer data output reporting the color spectrum, luminance, and radiance values for a given stimulation level.

2.2 Pupil Recording

The second component of the CPG is the eye-tracking unit. The eye-tracking unit is mounted similarly to the stimulating sphere using a polystyrene ring with embedded magnets. This allows the entire unit to easily clip on and off the goggle frame. The eye-tracking unit consists of a CMOS C-Cam-2A camera (CONRAD GmbH; Munich, Germany) and four infrared (IR) LEDs (GaAIAs Infrared Emitter IRL 81 A Siemens GmbH; Munich, Germany) all mounted on a vertical and horizontal sliding stage. With this adjustable stage our device can accommodate for different geometries of the patients head and allows allow the eye to be in appropriate viewing field for accurate data acquisition. The eye-tracking unit will connect to an integrated circuit (IC) that will power the IR LEDs and provide all electronics to drive and process the video out signal from the CMOS camera. This eye tracking IC also features a small dial where the intensity of the IR LEDs can me adjusted for maximal visualization of the pupil. This circuit then connects to the eye tracking software (SensoMotoric Instruments GmbH; Teltow, Germany) that will analyze pupil diameter, contraction/dilation velocities, and eye gaze.

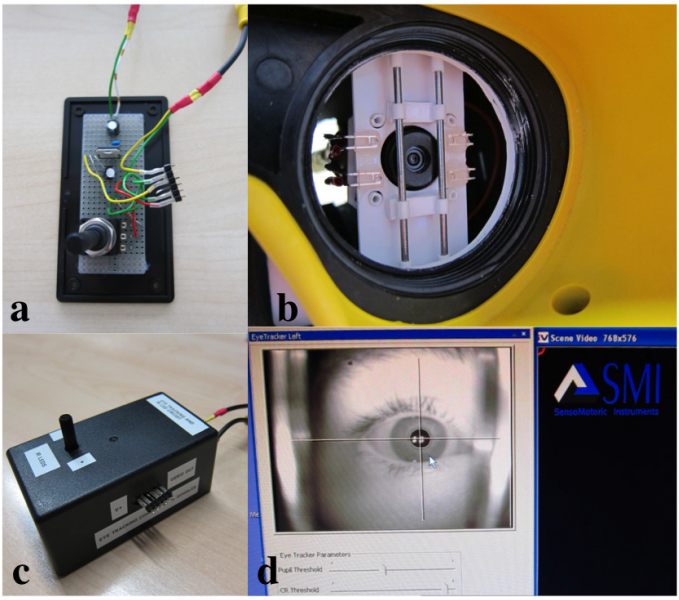

Fig. 5. a) Eye-tracking unit integrated circuit that consists of a voltage regulators, capacitors, resistors, and a potentiometer for adjusting the intensity of the IR LEDs. This circuit connects to power, the eye tracking unit, and the video in on the computer for SMI software to analyze the pupil response b) assembled eye tracking unit showing eye tracking camera, four mounted IR LEDs on the slidablehousing frame c) Eye tracking integrated circuit when sealed in enclosure; IR LED knob for modifying intensity and connectors for the eye tracking unit, video out, and power are visible d) eye tracking software during testing depicting white cross hairs that center on the pupil and place crosshairs that indicate the gazing direction.

2.3 ipRGC Stimulation Method

While the CPG is a versatile diagnostic tool that can execute many light stimulating protocols to activate a variety of cells with the pupil light reflex, our preliminary studies have focused on isolating the function of the ipRGCs. Using the PLR to study the function of the ipRGC can have many valuable clinical applications [3], [12]. An effective evaluation can aid in in determining the level of damage to the rentalphotocoreceptors compared with the retinal ganglion cells, the level at which ipRGCs regulate circadian rhythms in patients with minimal receptor function [13], and lastly determining if a patient has functioning retinal ganglion cells and can thus be a candidate for a retinal prosthesis[3], [14]. The lighting sequence is detailed in Fig. 6 and consists of two main stimulation methods, high intensity red light to stimulate the cones and high intensity blue light to stimulate the ipRGCs.

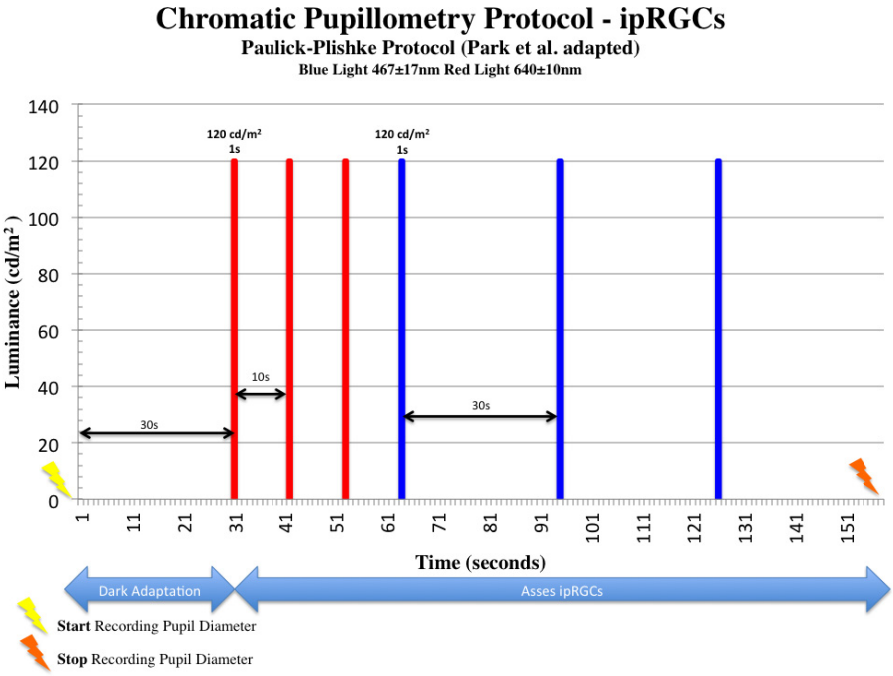

Fig. 6. Protocol used modeled after Park et al[3]findings to isolate the optimal stimulation sequence foripRGC function. This protocol uses a high intensity red light with a one second duration to stimulate the cone cells of the eye and a high intensity blue light to stimulate the ipRGC cells. The total testing time of this protocol is 2 minutes and 36 seconds.

3 Results

Preliminary validation of the pupillometry system has been conducted on ten different patients using the ipRGC protocol to assure the device and all corresponding data

analysis protocols are working properly. Patients were between the ages of 25 and 70 with no known ocular or visual problems. The chromatic pupillometer successfully stimulated the pupil light reflex at varying wavelengths and intensities while recording the pupil response. Patients reported the device was comfortable and the testing was simple and non-obtrusive and the testing sequence was not bothersome or too bright that it became uncomfortable.

Fig.7 demonstrates the raw data collected from one patient that was given the ipRGC protocol. This data is unfiltered and no artifact removal has been done. This data demonstrates the validation of the CPG successfully stimulating and recording the PLR.

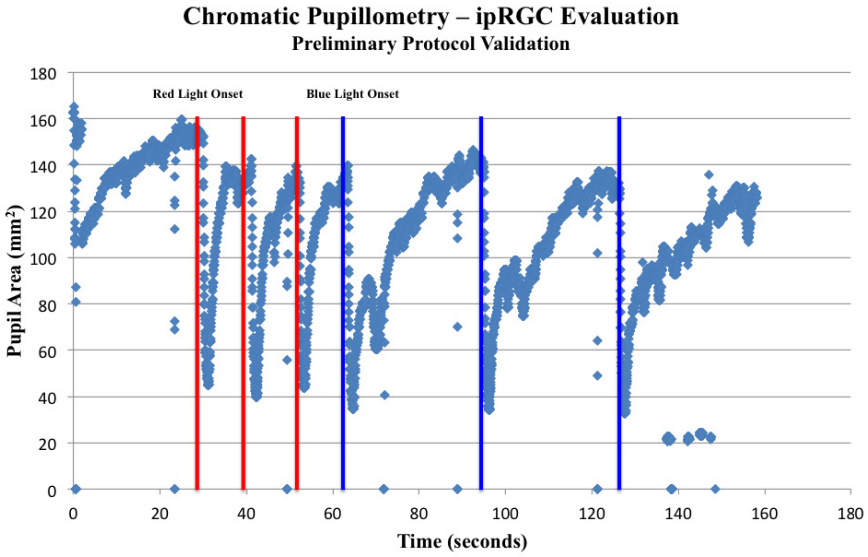

Fig. 7. Figuredisplays the raw and unfiltered pupil area data after stimulating the patients the PLC with the sequencedescribed in Fig.6.The patient blinked right as the test was beginning which explains why there is a decreased in pupil area directly at the beginning of the experiment before the lighting protocol had begun.

4 Discussion

Our group has developed a device for chromatic pupil response measurements to explore the pupil light reflex. This device is easy to use and comfortable for the patient to wear during testing. This compact system houses both the stimulating and the recording hardware for all measurements to be taken. Preliminary testing has demonstrated the repeatability of these measurements and is ready for a larger scale clinical trial to explore the complex PLR and specifically the function of the ipRGCs. The

preliminary experiments evaluating the ipRGC and cone function of the pupil light reflex have demonstrated the expected response profiles for healthy PLR. Specifically, high intensity blue light was able to produce a sustained pupil response, presumably a melanopsin driven sustained response, lasting approximately 30 seconds[3], [11] .Comparatively, the cone function assessment using high intensity red light demonstrated a response time (return to baseline) of approximately 10 seconds post stimulation. Our group is interested in conducting a large scale trial evaluating the function of ipRGCs over a wide range of ages to explore for the ipRGCs function changes over time. Moreover our group would like to establish a guideline for healthyipRGC response to use as anindicator for non-invasive diagnostic testing ofipRGC function.

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