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Development of a Non-Invasive Blink Reflexometer

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ABSTRACT Qualitative assessments of the blink reflex are used clinically to assess neurological status in critical care, operating room, and rehabilitative settings. Despite decades of literature supporting the use of quantitative measurements of the blink reflex in the evaluation of multiple neurological disorders, clinical adoption has failed. Thus, there remains an unmet clinical need for an objective, portable, non-invasive metric of neurological health that can be used in a variety of settings. We have developed a high-speed videography-based device to trigger, record, and analyze a blink reflex. A pilot study was performed to compare the device's measurements to the published literature of electromyographic measurements, currently the gold standard. The study results indicate that the device is a viable tool to obtain fast, objective, and quantitative metrics of a blink reflex, and has promise as a non-invasive diagnostic assessment of neurological health.

INDEX TERMS Blink, brain, reflex, concussion, diagnostic, imaging, neurology.

I. INTRODUCTION

Blinking is an activity that serves physiologic maintenance, protective, and brain restorative functions. With every blink, an ocular lubricant is swept across the eyeball providing moisture and anti-microbial protection to the orbit. Blinking also provides rest and reset for retinal cells that are activated and fade when fixed on an object. Blinks can be classified as voluntary, acquired, passive, spontaneous and reflexive; each with a distinct cause, innervation pathway and temporal profile.

Reflexive blinks, also called the blink reflexes, can be elicited by tactile, light, and sound stimulation, and serve to provide a first line of defense to the globe and the brain behind it.

In 1952, Kugelberg [8] performed the first electrical studies of the blink reflex in a normal population and described electromyography (EMG)-derived time metrics for each phase of eyelid movement. Numerous others [1]–[3], [7], [13]–[15] followed with studies examining the blink reflex in normal populations, as well as the changes that occur

in a variety of neurological conditions, such as Parkinson's disease [2], [7], Huntington's disease [2], schizophrenia [11] and severe traumatic brain injury [4]. Indeed, the sensitivity of the blink reflex to a variety of insults indicates that it may be a useful tool for assessing neurological function. This is particularly relevant given the current public interest in developing methods to detect concussions, offering a more encompassing field sobriety test, and monitoring patients for early onset of Alzheimer's disease. However, despite the correlation between altered blink reflex parameters and neurological health, quantitative approaches for examining the blink reflex have never been adopted in clinical practice, and qualitative assessments remain standard.

During the six decades since Kugelberg first quantitatively described blink reflex time metrics, considerable technological advancements have been made. Digital image capture technologies have improved significantly over the past two decades and have significantly decreased in cost. The high frame rates currently available allow for measurements in the millisecond range, necessary for quantifying blink reflexes.

Concurrently, processing power has increased making analysis of the thousands of image frames recorded at high frame rates feasible. High-speed image capture has been successfully employed to record and measure eyelid location during a single, voluntary blink in both healthy subjects [9] and in patients with blepharoptosis [10]. However, to the authors' knowledge, no study has used high-speed image capture to study reflexive blinks.

This paper describes a portable blink reflexometer that triggers, records and evaluates multiple reflexive blinks quickly, non-invasively, and objectively.

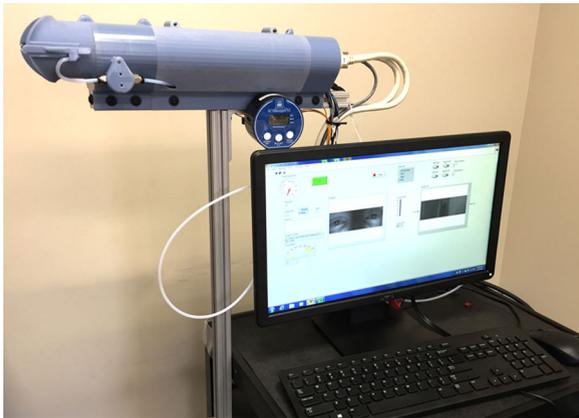


FIGURE 1. Blink reflexometer housing unit and software interface. Tubing connected to the left end of the housing unit delivers a puff of compressed air to the subject's eyes.

II. METHODS AND PROCEDURES

A. DEVICE

The blink reflexometer (Fig. 1) consists of a mask, a housing unit, a stimulation system, a camera, an external controller and processor, and a user interface.

The mask is composed of flexible material configured to fit against the face of the subject to block out external light and minimize distractions.

The housing of the blink reflexometer contains several components (Fig. 2). It has a center barrier used to prevent inadvertent stimulation of the eye contralateral to the nozzle delivering the CO₂ puff. At the back of the housing is a mirror used by the subject for vertical centering of his reflection such that the eyes are aligned in the center of the image frame and aligned with the stimulus nozzle.

The stimulation system shown in Fig. 1 randomly delivers a puff of compressed air to either the right or the left eye. The air puff is generated from an external air-compressor (TCP Global, San Diego, CA) connected via solenoids (Clippard EV-2-12, Clippard Instrument Laboratory, Inc., Cincinnati, OH) to nozzles in the housing unit through a polyethylene tube. The nozzles are adjustable and aimed such that the air puff is delivered to the outer canthus of the subject's right or left eye. Microphones (CME-1538-100LB, CUI Inc., Tualatin, OR) are positioned at the exit of the nozzle to capture the sound of the air exiting. The microphone recording

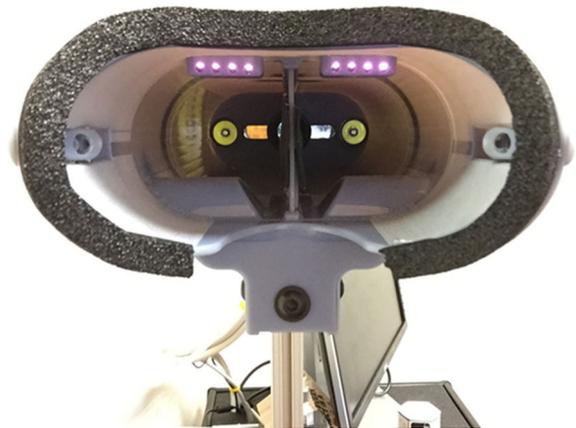


FIGURE 2. The housing unit has a center barrier to prevent inadvertent stimulation of the contralateral eye. Two arrays of IR LEDs provide scene illumination.

provides a time stamp of stimulation delivery to the eye, which is used for blink reflex parameter calculations.

An array of infrared light emitting diodes (XTNI30W, SunLED, Walnut, CA) is located on each side of the barrier to illuminate the cavity. The array also creates a reflection pattern on the subject's irises and pupils that can be used to automatically locate the eyes in an image frame.

A camera (GZL-CL-22C5M-C, Point Grey Research, Richmond, BC, Canada) is mounted to a rigid frame facing the subject's face, centered and aligned with the subject's eyes vertically. It captures high-definition grayscale images at 280 frames per second with a frame size of 1400-by-500 pixels.

A custom user interface (LabVIEW v13.0.1, National Instruments, Austin, TX) allows the test administrator to control several functions including number of stimuli delivered and duration of the test. A random number generator is used to determine the order of stimuli delivery to each eye of the subject based on the number of stimuli specified by the test administrator. The interface also starts the test and collects subject information for reference. Image frames along with sensor and stimulus data are recorded to hard disk.



FIGURE 3. Location of the upper right (red dot) and left (blue dot) eyelids are located in each image acquired during a blink.

B. DATA PROCESSING

The edge of the both eyelids is detected using custom software (LabVIEW) (Fig. 3). The program then tracks, using an

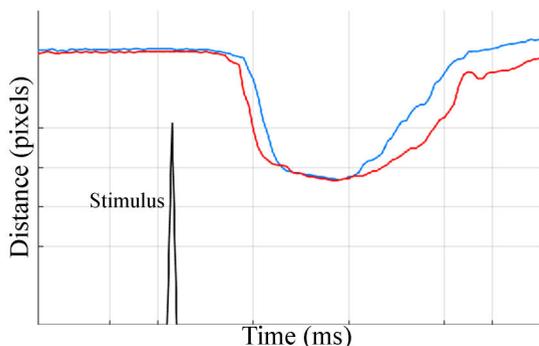


FIGURE 4. Eyelid excursions of the right (red trace) and left (blue trace) eyelids during a single stimulated blink. An air puff stimulus was delivered to the right eye (ipsilateral), which begins closing before the left (contralateral) eye.

edge detection algorithm, the vertical positions of each eyelid through the entire image sequence.

For each eyelid, pixel location per frame is used to chart eyelid movement (Fig. 4). Microphone data are synchronized with image data based on sampling frequency.

From the displacement profile for each eyelid, several blink parameters are calculated (TABLE 1).

TABLE 1. Blink parameters calculated.

Parameter	Description
Latency	Time between stimulus to first eyelid movement
Differential Latency	Difference in start time between eyelids
Duration	Time from start of eyelid movement to eyelid open

C. PILOT STUDY INVESTIGATING FEASIBILITY OF NON-INVASIVE, IMAGE-BASED BLINK MEASUREMENTS

To validate the measurements obtained with the blink reflexometer to published literature using EMG, a pilot study was conducted.

Using an IRB approved protocol ten subjects (8 male, 2 female; Age: 19.6 +/- 1.58 years) were recruited from The Citadel (Charleston, SC) student body. None of the subjects had a history of brain surgery, epilepsy, Parkinson’s disease, stroke, Alzheimer’s disease, brain tumor, aneurysm, cranial nerve palsies, blepharospasms, glaucoma, or current symptoms of dry eye, corneal abrasions/lacerations, or conjunctivitis.

Each subject had between one and four test sessions. Each session consisted of two or three twenty-second tests in which one to five air puff stimuli were randomly delivered while images were recorded (280 frames per second = 3 ms resolution). Movement of each eyelid counted as a separate blink event, i.e., closing both the right and left eyelid constitutes two blinks for data analysis.

Data were excluded if the eyelid was already in motion upon stimulus delivery. If the eyes were closed at the start of

TABLE 2. Subject data collection.

Subject	Sessions	Tests	Stimulated Blinks	Excluded Blinks
6151	1	3	28	3
6107	2	2-3	41	11
6073	3	3	79	13
6097	3	3	86	8
6030	3	3	88	9
6168	3	3	82	17
6114	3	2-3	77	9
6028	3	3	82	6
6104	4	2-3	117	16
6113	4	2-3	64	8

TABLE 3. Comparison of blink reflexometer measurements with published literature.

	Median (IQR ⁺)	Published Range	Proportion Variability Due to Subject
Latency (ms)	51 (12)	40-70*	0.09
Differential Latency (ms)	4 (7)	~ 12**	0.07
Duration (ms)	177 (94)	~200**	0.19

*Esteban, 1999 [2]; **Helmchen and Rambold, 2007 [7]
⁺IQR =inner-quartile range = 75th – 25th percentile values

data recording, they were manually located in a subsequent frame and the data analysis began at that frame.

III. RESULTS

The image capture rate used in this study is lower than what has been previously used [9], [10] for eyelid tracking (600 fps). Despite the lower capture rate, the software was successfully able to locate the eyelids in each frame and track excursion.

Based on availability, subjects had between one and three test sessions (2 subjects had 4 sessions, 7 subjects had 3 sessions; 1 subject had 2 sessions; 1 subject had 1 session; TABLE 2). Of the 744 stimulated blinks recorded, 100 blinks were excluded (TABLE 2).

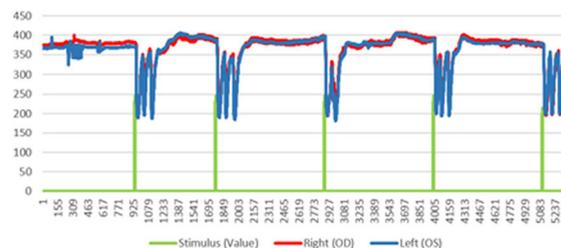


FIGURE 5. Representative right (red) and left (blue) eyelid excursion graph for one subject during one twenty-second test. Green lines indicate stimulus delivery.

As seen in Fig. 5, some subjects tended to blink multiple times after stimulus delivery. However, only the first blink elicited by the stimulus delivery was used in the data analysis.

Consistent with published literature [2], [12] intra-subject variability was low (TABLE 3, proportion of variability due to the subject). For the three blink parameters assessed, measurements by the blink reflexometer are consistent with the published literature (TABLE 3). Only Differential Latency fell slightly outside of the published range.

IV. CONCLUSION

The blink reflexometer described in this manuscript was developed to trigger, record and evaluate reflexive blinks. The device integrates stimulation and recording modalities, as well as evaluation metrics, selected based upon the knowledge acquired from blink reflex studies performed over the past 65 years.

Tactile stimulation, in the form of a puff of air, was selected to trigger the reflex because the probability of eliciting a response approaches 1.0 [5]. Subjects did not complain about the puff being uncomfortable, but did blink multiple times after receiving each stimulus. Air puff stimulation can introduce acoustic artifacts, which may impact the results [6]. Light or sound could alternatively be used to trigger a reflexive blink, but each has its own limitations for use.

This pilot study confirms that the blink reflexometer is capable of providing non-invasive, quantitative measurements of the blink reflex consistent with prior EMG-derived data. It should be noted that the subject population in this study was limited to a small sample of young, healthy, college students. The applicability and accuracy of the blink reflexometer needs to be tested in a subject pool more closely matching the normal population before its measurement validity and its utility as a potential clinical tool can be fully assessed.

Even with a larger subject pool, the adoption of quantitative measures of the blink reflex may still be limited. More research is needed to validate the usefulness of the reflex and this technology in each area of clinical need. The cost of the research and of the technology itself may prove a barrier. Additionally, the technology presented here is intended to be a tool useful for detecting changes in the blink reflex that are correlative to neurological state. Like the thermometer, the blink reflexometer is not designed for or capable of detecting the underlying causality for the change. The lack of causal information may be the reason that quantitative measurements of the blink reflex are not currently used clinically, and increasing the ease and speed of the measurement tool may not improve clinical adoption.

Despite the above noted limitations, the blink reflexometer presented here is a non-invasive, functional technology

with the potential to make the blink reflex another vital sign or metric considered in the normal course of medical examinations.

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STATEMENT OF FINANCIAL INTEREST

The blink reflexometer described in this article is patent pending and available for investigational use only. The Medical University of South Carolina, the Zucker Institute for Applied Neurosciences, and authors Tsai, Semler and Kothera have financial interest in the technology.

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