Pupillary Light Reflex: A Clinical Tool for Early Detection of mTBI/Concussion

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Background

There is an increase in mild traumatic brain injury (mTBI) in US Warfighters resulting from exposure to explosive devices. The Department of Defense reported that 273,859 new cases of TBI have been clinically confirmed from 2000 to the first quarter of 2013, with mTBI accounting for 82% of all cases. However, there is a lack of objective biomarkers to accurately identify mTBI in order to make a return-to-duty (RTD) determination in the battlefield. Cognitive and neurosensory abilities potentially degraded by mTBI are crucial for military personnel in combat since their lives and safety depends on accurate and rapid situational awareness and perception of the environment. Prompt and accurate diagnosis and management of mTBI increases an individual's prognosis for neurological recovery and safe RTD. The present study examined pupillary light reflex (PLR) as a potential objective biomarker for early identification of mTBI.

Methods

Forty U.S. military personnel participated in this study, equally divided in two groups: blast induced-mTBI group and non-TBI group. The blast-induced mTBI subjects were recruited during the subacute stage, i.e., between 15 and 45 days post-injury and receiving medical care at Walter Reed Army Medical Center (WRAMC). The age-matched non-TBI subjects who had deployed, but had no history of TBI or concussion were tested at the U.S. Army Aeromedical Research Laboratory. Subjects in the blast-induced mTBI group had a documented history of mTBI based on the criteria of the American Congress of Rehabilitation Medicine: 1) loss of consciousness of no more than 30 min; 2) post-traumatic amnesia of no more than 24 hours; 3) a Glasgow Coma Scale from 13 to 15; 4) alteration of mental stage. For this study, "blast-induced mTBI" included mTBI caused by improvised explosive devices, rocket propelled grenades and mortars. Subjects in the mTBI group were enrolled regardless the level of symptomatology. The study protocol was approved by the U.S. Army Medical Research and Materiel Command Institutional Review Board and the WRAMC Department of Clinical Investigation. All subjects underwent a comprehensive medical history review and eye examination to determine refractive error and ocular health using standard clinical procedures.

The PLR-200™ (NeurOptics, Irvine, CA) monocular infrared pupillometer (**Fig. 1A**) was used to quantify PLR under mesopic conditions (approximately 3 cd/m2). Monocular PLR measurements were taken under binocular viewing conditions. The subject fixated with the non-tested eye on a distance target located at 10 ft away to avoid changes in pupil size due to accommodation and to prevent recording artifacts by blinking during PLR recordings. The PLR was recorded twice in the right eye and then twice in the left eye with an interval of about 30 sec between recording. The pupillometer presented a 180 microWatts light stimulus for 167 milliseconds and captured PLR using a 32-frames per second sampling rate. Eight PLR parameters were assessed: maximum diameter; minimum diameter; percent of constriction; constriction latency; average constriction velocity; maximum constriction velocity; 75% recovery time; average dilation velocity. **Figure 1B** illustrates a schematic of the pupil response curve and PLR recorded parameters.

Keywords: Military; Pupil; Pupillary Light reflex; PLR; Pupillary dynamics; Mild traumatic brain injury; mTBI; Blast

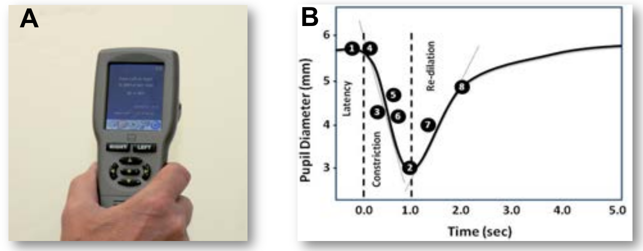

Figure 1: **(A)** PLR-200™ monocular infrared pupillometer. **(B)** Schematic diagram of the pupillary reaction curve illustrating recorded PLR parameters: 1) maximum diameter; 2) minimum diameter; 3) percent of constriction; 4) constriction latency; 5) average constriction velocity; 6) maximum constriction velocity; 7) average dilation velocity; 8) 75% recovery time.

Results

This study compared PLR of 20 Warfighters with mTBI (14 males; 6 females) during the subacute stage post blast injury and 20 age-matched controls (18 males; 2 females). The participants' mean (SD) age was 31.2 (7.4), ranging from 20 to 43 years. All subjects were corrected to 20/20 and had similar spherical equivalent refractive error (mTBI -0.49 ± 2.07 D; non-TBI +0.12 ± 0.98 D; p = 0.25). All subjects had normal pupil response and no afferent pupil defect with manual penlight examination. Four of 8 PLR parameters were statistically significant between groups: constriction latency, average constriction velocity, average dilation velocity and 75% recovery time (**Figs. 2 and 3**).

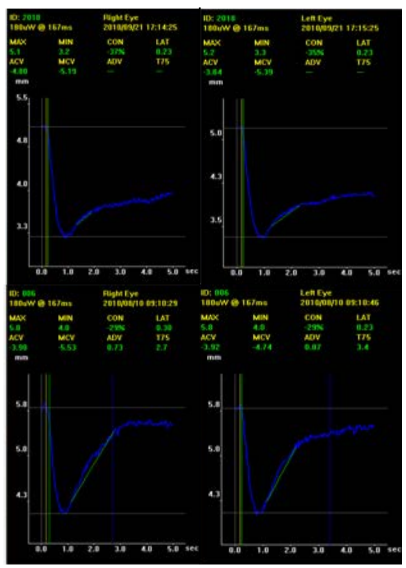

Figure 2: Images of the typical pupillary response curve for a subject with blast-induced mTBI (upper panels) and age-matched non-TBI (lower panels).

Note:
MAX = maximum diameter
MIN = minimum diameter
CON = percent of constriction
LAT = constriction latency
ACV = average constriction velocity
MCV = max constriction velocity
ADV = average dilation velocity
T75 = 75% recovery time

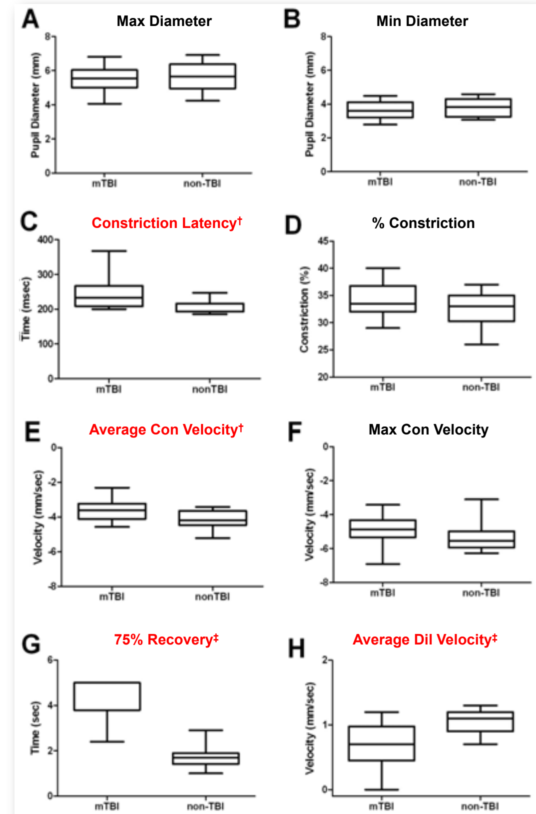

Figure 3: Summary of PLR parameters for mTBI and non-TBI groups. A box and whisker plots is shown for each PLR parameter: bottom and top of the box are the 1st and 3rd quartiles, and the band inside the box is the median. †p <0.05; ‡p <0.001.

Conclusions

This study demonstrates the potential application of the PLR as an objective biomarkers to expedite the diagnosis of mTBI in the battlefield and to facilitate the RTD decisions by deployed healthcare providers.

References

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