Pupillary responses to offset and onset of isolated rod and cone stimuli using a 4-primary photostimulating method

Frederick T. Collison¹, Dingcai Cao², J. Jason McAnany², Mohamed A. Genead¹, Gerald A. Fishman¹,²
¹ The Pangere Center for Hereditary Retinal Diseases, The Chicago Lighthouse for People who are Blind or Visually Impaired, Chicago, IL, USA. ² Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, IL, USA.

INTRODUCTION

- The pupil paradoxically constricts at light offset in some patients with achromatopsia and complete congenital stationary night blindness. (1) Transient pupil constrictions to overall light decrement can be elicited in subjects with normal vision viewing chromatic stimuli. (2)
- Intrinsically photosensitive retinal ganglion cells provide afferent input for the pupillary light reflex and depolarize at light onset. (3,4)
- Along with their intrinsic photosensitivity, ipRGCs receive input from rods and cones via bipolar and amacrine cells.

METHODS

- Stimuli
  - A commercially available four-primary photostimulator (Diagnosys ColorDome) was used to generate the rod and cone (L+M+S) isolated stimuli shown in Table 1.
  - The studied eye was patched for 5 minutes prior to testing. Each trial started with a 30 second adaptation to the background (L+M+S + Rod), followed by alternated decrement stimuli (10 sec) and background (10 sec), with each stimulus repeating 5 times.

- Pupil Measurement
  - Monocular pupil responses were recorded using a frame-mounted infrared pupillometer (Arrington Research, resolution 0.03 mm 60 Hz). A 0.5 second median filter was applied to all pupil recordings.
  - Measurements of baseline, transient minimum, and sustained pupil diameters are shown in Figure 1. Percentages of constriction were calculated versus baseline.

- Subjects
  - Ten visually normal subjects (age range 24-41) were tested at 100 cd/m².

- Statistics and Validation
  - Differences among the conditions were evaluated using non-parametric Wilcoxon signed-rank tests.
  - Average pupil size after light change (Transient Change) was calculated vs baseline to verify small transient constriction.
  - The cone isolation (L+M+S) stimulus was reported not visible by three patients with rod monochromatism (one incomplete, two complete). All three achromats found the Rod and S-cone isolating stimuli to be visible.

RESULTS

- Averaged percent transient constrictions, significance and for all stimuli are shown in Table 1.

- For isolated S-cone stimuli at 100 cd/m², the pupil constriction to decrement was greater than to increment (17.2% decrement vs. 10.6% increment constriction, p = 0.0199; example in Figure 1). For isolated rod, isolated L+M+S, and overall L+M+HS luminance changes at 100 cd/m² and at 10 cd/m² (isolated rod) increment constriction was greater than decrement constriction (all p values < 0.05). At 1.25 cd/m² the isolated rod increment constriction was not statistically greater than the isolated rod decrement constriction.

- No significant difference was found between 5 and 20 minutes DA prior to 1.25 cd/m².

- Sustained responses to isolated stimuli were near zero, without significant constriction, except for a small sustained constriction to Rod increment at 100 cd/m² (3.07%, p = 0.0125), possibly due to the influence of melanopans.

- Using our isolated stimuli, we reliably elicited transient pupil constrictions to rod, L+M+S cone, and S cone onset, as well as to S cone offset. Small constriction were found to isolated rod and L + M cone offset.

- S cone OFF constriction was greater than equal to S cone ON constriction for all subjects, consistent with the finding of previous investigators of S cone OFF depolarization of ipRGCs in the macaque retina. (6) The S cone isolating stimulus produces robust ON and OFF responses in normals, making it a potentially good test for blue-yellow pathway loss and blue cone loss. The finding of rod-isolated transient pupil responses at mesopic and photopic luminance levels could lead to clinical tests of rod function that save the time of dark adaptation.

- With the finding of similar responses with 5 and 20 minutes of dark adaptation prior to 1.25 cd/m² rod isolated stimuli, the rod isolated pupil stimulus could be a useful clinical tool that avoids the need for full dark adaptation.

REFERENCES


SUPPORT

Pangere Corporation; Grousbeck Foundation; NIH R01EY019561 (DC); NIH R01EY019561 (JM).