REVIEW ARTICLE

RAPDx Expanded Pupil Diagnostics: A new Dimension in Pupil Evaluation

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ABSTRACT

Introduction: Relative afferent pupillary defect (RAPD) is an imperative sign to assess the retinal and optic nerve function. However, RAPD is subjective, so leads to discrepancies and hence there is the need for a precise quantification of the same.

Materials and Methods: 80 subjects were enrolled in the study, pupillary reactions were measured using RAPDx Expanded Pupil Diagnostics (Konan Medical USA, Inc., Irvine, CA, USA) and were compared with neutral density filter (NDF) (Gulden Ophthalmics) and swinging flashlight test.

Results: The mean pupillary reactions assessed on NDF was less than 0.3 log units and that assessed on RAPDx was 0.28 log units (P<0.001 spearman's coefficient).

Conclusion: RAPDx is comparable to NDF and may be used as a screening tool in Ophthalmology clinic, and gives an accurate and precise quantification of pupillary responses.

KEY WORDS: Pupil Diagnostics, RAPD, RAPDx

INTRODUCTION

Relative afferent pupillary defect (RAPD) is caused by lesions of the anterior visual pathway, produce asymmetric inputs, into the pupillomotor zone of the brain, as first described by Levatin in 1959.[1,2] Abnormalities in the pupillary light reflex can be detected by alternately illuminating each eye while comparing the change in pupil size.[3] Asymmetry in this response is referred to as RAPD.

RAPD is an established way of assessing retinal and optic nerve function.[4,5] Subjective grading leads to discrepancies among clinicians, is difficult to quantify, and limits its use in diagnosis.

Various techniques have been described to quantify or measure RAPD. These include the use of neutral density filters (NDF),[3] cross polarized filters,[6] and subjective grading based on the amount of initial contraction and subsequent redilation of each pupil as the light is swung.[7,8]

RAPD has typically been assessed quantitatively with the swinging flashlight test,[9] using an NDF placed in front of the better eye in 0.3 log10 steps.[3] However, this test presents several problems, including end-point determination, unequal retinal illumination, and examiner bias. Furthermore, it is difficult to evaluate RAPD with the swinging flashlight test in patients with dark irides or small or poorly reactive pupils.[10,11]

RAPD can be quantified by sequentially placing optic filters of increasing density in front of the normal eye as a light source alternately illuminating each eye. RAPD can be detected when there is approximately 25-50% unilateral loss of retinal ganglion cells.[13] Compared to this method,[12] Chang *et al*. concluded that RAPDx automated infrared pupillograph allows for more precise quantification of the pupillary response using controlled stimulus intensities, and this has improved the ability to detect and objectively quantify subtle RAPDs.[14,15] Tatham

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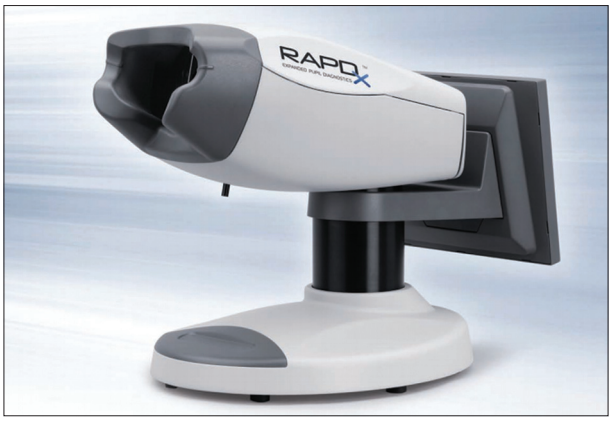
et al. concluded in their study that RAPDx provides an accurate measurement of pupillary light reflex.[16]

Procedure

The automated pupillometer (RAPDx; Konan Medical USA, Irvine, California, USA) was used to record and analyze the pupillary light reflex. Each subject was dark adapted for 1 min before the test. RAPDx measurements were taken in a dark room. The screen displayed a target (green cross) for patient fixation and viewed at infinity through a pair of 50 mm objective lens. During the test, the subject was not required to wear any glasses or refractive correction. The device incorporates pupil tracking and blink detection systems using 60 full-frames/s digital cameras, each with a resolution of 240 × 240 pixels/frame, for approximately 25 pixels/mm. If a blink obscures the pupil during recording, the test is repeated automatically. While the patient views binocularly, varied types of stimuli are presented on the LCD panel, alternating between eyes (similar to the swinging flashlight test).



Stimuli of varied colors (white, red, green, blue, and yellow); of varied patterns (full-field, peripheral [28° with 10.5° macular sparing]); central (2.9°); superior and inferior nasal quadrant arcs (21° with 11.7° macular spacing); and of varied intensities (35 lux [bright] and 25 lux [dim]) can be used. All stimulus cycles add up to 2.1 s, with full-field stimulations of 200 ms followed by 1900 ms dark and patterned stimulations of 600 ms followed by 1500 ms dark. The entire examination lasts approximately 7 min.

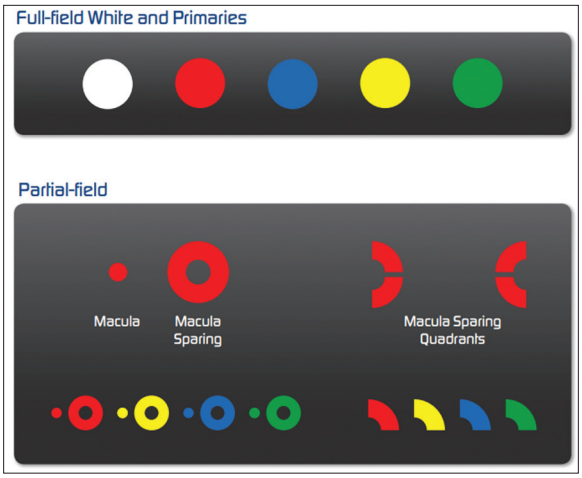


Image Courtesy: RAPDx Brochure

The device records pupil diameter over time and calculates 6 metrics (response amplitude, latency, maximum constriction velocity, maximum dilation velocity, and time to peak constriction and dilation).[13]

The area of stimulation is 30° of the visual field. The stimulus colors are not completely saturated, and the peak emissions are as follows: Red 605 nm, Green 555 nm, Blue 440 nm, and Yellow 576 nm.[2]

Pupil response parameters

The pupillograph generates pairs of simultaneous biometric waveforms that describe the average pupil responses (combined right and left eye) to the monocular stimuli. Software is incorporated to parse the pupil diameter waveforms into specific metrics. The median value from the series of repetitions is calculated to minimize noise. Parameters measured by the pupillograph include response amplitude (RespAmp), which is the maximum contraction of the pupil as a percentage of the prestimulation size, that is, the prestimulus pupil diameter minus the minimum pupil diameter, divided by the prestimulus pupil diameter; response latency (RespLat), which is the time in milliseconds between stimulus onset and time when pupil velocity has reached 50% of the peak velocity of constriction; maximum velocity of constriction (ConMaxVel); latency of the maximum velocity of constriction (ConMaxVelLat); maximum velocity of dilation (DilMaxVel); and latency of the maximum velocity of dilation (DilMaxVelLat).[11]

An index of the direction and magnitude of pupil response asymmetry, known as the RAPD score, is generated automatically by the pupillograph. The RAPD score is calculated as the difference in the amplitude of pupil constriction between stimulation of the 2 eyes using the following formula: 10*log10 (amplitude of OD/amplitude of OS) (OD, right eye; OS, left eye). The latency is the interval between the beginning of the stimulus and the detection of a significant pupil velocity, which is considered to be the onset of the reflex. The RAPD latency score is the 10*log10 (latency of OD/latency of OS).[2]

Here, OD is the mean response amplitude of both pupils in response to right eye stimulation, and OS is the mean response amplitude in both pupils in response to left eye stimulation. A positive value indicates a relative abnormality of the left afferent system and a negative value indicates a relative abnormality of the right afferent system.[17]

RESULTS

In our pilot study on 80 normals, age group of 10-60 years, subjects without any known ocular pathology, the pupillary reactions were measured using RAPDx Expanded Pupil Diagnostics (Konan Medical USA, Inc., Irvine, CA, USA) and were compared with NDF (Gulden Ophthalmics). Ametropia was not an exclusion criterion in our study, as the patients do not need to wear any refractive correction during the test. The stimuli was projected at infinity by a pair of objective lens.

The subjects were dark adapted for 1 min and then the swinging flashlight test was performed, and findings noted, followed by pupillary assessment by NDF and then the RAPDx. All the three tests were performed by separate blinded investigators and findings noted.

The mean pupillary reactions in 80 normals (57% males, 43 females) assessed by NDF was found to be less than 0.3 log units. On RAPDx, the same was found to be 0.28 log units. Statistically significant correlation ($P < 0.001$) was seen between the two, assessed by spearman's rank correlation coefficient.

DISCUSSION

On swinging flashlight test, only the presence or absence of RAPD can be assessed. However, this is subjective, and the findings are highly variable.

On NDF, the RAPD if present can be graded as 0.3,0.6, 0.9 log units and so on, which is again highly subjective and is a combination of swinging flash light test with the graded log scale, i.e. NDF.

RAPDx is an automated tool, which records the pupillary reactions by providing monocular stimuli and then recording the direct and indirect pupillary reflexes simultaneously to multiple stimuli and finally gives a score including the amplitude of the reaction with the latency of the same.

LIMITATION

However, pupillary assessment on RAPDx may detect RAPD only in asymmetrical optic nerve or retinal pathologies as RAPD is seldom seen in symmetrical disease processes.

CONCLUSION

This pilot study concludes that RAPDx is more specific when compared to NDF in measuring RAPD.

An advantage of the automated pupillograph is that it is possible to obtain multiple pupil response characteristics to multiple stimuli. Furthermore, because the device is computerized, it would be possible to generate an index automatically. The magnitude of pupil response asymmetry is termed as RAPD score.

Thus, RAPDx gives an accurate and precise quantification of pupillary responses.

RAPDx may prove to be helpful in assessing patients with asymmetric disease of the optic nerve and retina. As RAPD is a marker of an asymmetric impairment of the afferent visual system.[18]

Hence, RAPDx may be used as a screening tool in ophthalmology clinic.

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