

Article • Use of Dyop Colors Test for Color Acuity Assessments

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ABSTRACT

Background: This paper addresses the concept of using a form of dynamic optotype called a Dyop (pronounced “di-op”), both colored and black-on-white, in subsets of the population. The ability to detect specific acuity endpoints in primary colors has numerous potential implications. Red (L) with a peak at 575 nm, Green (M) with a peak at 535 nm, and Blue (S) with a peak at 449 nm have indications in easy detection of medical conditions such as glaucoma, dyslexia, and/or ADHD. The present study investigated the clinical significance of color acuity (CA) in dyslexia, ADHD, preperimetric glaucoma (PPG), and open-angle glaucoma (OAG).

Methods: A total of 251 eyes of 204 subjects (29 dyslexia eyes, 10 ADHD eyes, 22 PPG eyes, 23 normal-tension glaucoma (NTG) eyes, 23 primary open-angle glaucoma (POAG) eyes, and 144 normal eyes as a control group as well as for initial Dyop CA validation, aged 27.83 ± 14.44 years, 6-72 years) were enrolled. Dyop basic visual acuity (VA) and Dyop CA endpoints, as well as VA and CAs for refraction corrected with +2.00 lens and +3.00 lens of blur using standard spherical lenses for normal eyes, were recorded. Then, basic VA and CAs were evaluated for blue-on-gray (BOG), green-on-gray (GOG), yellow-on-gray (YOG), and red-on-gray (ROG) in the various groups.

Results: The CA comparisons of the four colors were significantly different from the basic Dyop acuity irrespective of gender, left or right eye, and increasing diopter of 2 D and 3 D blur. The eyes with dyslexia and ADHD had the best CA in GOG

and ROG, respectively, while ROG and BOG were detectably impaired in eyes with NTG (ROG: 20 arc minutes or 6/30 and BOG: 24 arc minutes or 6/45) and POAG (ROG: 24 arc minutes or 6/45 and BOG: 28 arc minutes or 6/60), in very close association ($p < 0.05$) with a degree of functional loss, but GOG and YOG were not impaired in these eyes and not associated with glaucoma severity, POAG (GOG: 12 arc minute or 6/14; YOG: 8 arc minutes or 6/6) and NTG (GOG: 11 arc minutes or 6/12; YOG: 9 arc minutes or 6/7.5). However, there is a significant association ($p < 0.05$) between BOG, ROG, and GOG assessed in PPG and depletion of retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC), which was not seen in the control group.

Conclusions: Green and red CAs were detectably best in dyslexia and ADHD, respectively. Blue and red were detectably worse in eyes with glaucomatous optic neuropathy and in close association with the degree of functional loss. These findings suggest that measuring CA with the new Dyop colors test as described may be a very effective and efficient supplement to the existing methods of detecting dyslexia, ADHD, and glaucoma, as well as evaluating the severity of these diseases.

Keywords: ADHD, color test, Dyop, dyslexia, NTG, POAG

Introduction

The human visual system has the capacity to process both chromatic (i.e., color) as well as achromatic (visual acuity and contrast sensitivity) information, which is assessed conventionally in clinics.^{1,2} The ability of the eye easily to resolve the distinct colors of objects, known as color acuity (CA), might not be the same in all humans, especially with specific anomalies or acquired eye diseases.^{3,4} Vision scientists and eye care professionals still calibrate visual clarity (acuity) in only black and white, despite the obvious reality that most people see in colors.

The “global standard” for that black/white acuity is the 1862 developed Snellen test,⁵ which ignores the chromatic nature of vision and the fact that vision is actually a dynamic rather than a static process. The

inherently static optotype fixation of Snellen leads to a photoreceptor response depletion and a tendency for an overminus measure of acuity/refractions.^{6,7}

A Dyop (pronounced “di-op,” short for dynamic optotype) is a spinning segmented ring used as a visual target (optotype) to measure acuity (visual clarity) and for refraction. The smallest diameter spinning Dyop ring whose direction of spin can be detected is the acuity endpoint (visual clarity benchmark). When the contrasting gaps/segments of the spinning Dyop are smaller than the perception area of the photoreceptors (visual sub-acuity), the spinning gaps are too small to detect the Dyop rotation direction.^{6,7} Dyop arc minute diameter values were used for data comparison because they are a more rational and less culturally dependent measure of acuity, as well as more precise/accurate than traditional Snellen/LogMAR values.

The dynamic process of vision enables us to make sense of what we see, utilizing the vibratory motion of the visual saccades to refresh the response of the photoreceptors in the back of the retina. That refresh allows images to be dynamic and autonomic as the inner surface neurons of the retina function as the equivalent of a biological circuit board.^{7,8} The constant motion of the saccades allows the blue, green, and red cone-shaped photoreceptors to be constantly in adjustment in order to enable the chromatic triangulation of their focal depths to regulate acuity.⁹

The combination of the acuity responses from the individual red, green, or blue photoreceptors is turned into a matrix response by the inner neuroganglia layer of the retina.^{8,10} That cone photoreceptor stimulus is subsequently transmitted to the brain by the optic nerve fibers, where the response of 100 photoreceptors results in the stimulus provided by each optic nerve fiber.¹¹

Because the tubular-shaped cone photoreceptors have their sensitivities to color in the back of the retina, that tubular shape also modulates the intensity of the light reaching the rear of the cone photoreceptors, providing an added ability for motion detection of the target image. However, the programming function of the retinal neuroganglia is best exemplified by the Dyop MAR of 0.54 arc minutes squared, which correlates to 20 cone photoreceptors.^{10,12}

A spinning Dyop also enables easier acuity measurement in children and infants since children and infants have a preference for motion detection. The Adult Dyop test has two central Dyops, with only one of them spinning. A child or infant detecting the peripheral location of a spinning Dyop does NOT

require literacy and is done by watching their eye and head tracking movements. A Dyop can also be used to measure acuity in color—Red (L) with a peak at 575 nm, Green (M) with a peak at 535 nm, and Blue (S) with a peak at 449 nm—for possible diagnostic indications of potential signs of dyslexia, ADHD, migraines, epilepsy, or glaucoma. The Child Dyop test has two peripheral Dyops, with only one of them spinning. The Infant Dyop test has only one peripheral spinning Dyop, which changes peripheral location to attract the infant’s attention. The non-verbal objectivity of eye and head tracking illustrates the advantages of using a Dyop rather than static letters to measure acuity.^{13,14}

There is still a crucial controversy as to the diagnosis, prevalence, comorbidity, and treatment of the two most common developmental disorders in childhood: ADHD and reading disorder or dyslexia.¹⁵ The International Dyslexia Association defines dyslexia as a specific neurological learning disability, characterized by difficulty with inaccurate and fluent word recognition, poor spelling, and decoding problems. These difficulties stem from a deficiency in the phonological component of language and are often unexpected in relation to other cognitive and academic skills.^{16,17} Collateral consequences may include problems with reading comprehension and acquisition of knowledge, which could impede vocabulary growth and base knowledge.¹⁸ On the other hand, there is no agreed-upon definition of ADHD, but it is usually considered to be a persistent pattern of inattention and/or more severe hyperactivity-impulsivity and a frequency more than what is normally observed in subjects of a similar level of development, with some of these symptoms appearing before the age of 7 years and with clear evidence that they interfere with the subject’s social, academic, or work activity.¹⁹

Stein and Walsh^{20,21} have opined that the behavioral reading deficits are from a magnocellular system malfunction. The magnocellular theory, reformulated as a general temporal processing deficit in dyslexia recently,²⁰⁻²⁴ suggests that individuals with dyslexia have specific deficits in the processing of rapid visual and auditory stimuli.²⁵ Ideally, the magnocellular pathway is not involved in color vision, but it receives input from the three types of cones that are sensitive to different wavelengths of light, referred to as short (S; blue color), medium (M; green color), and long (L; red color) wavelength cones. In the same vein, it is opined that reading is compromised in red-light (long-wavelength) environments compared to green-light

(medium-wavelength) environments because red light inhibits the activity of the magnocellular system.²⁶

To the contrary, Fuermaier et al.²⁷ and Roessner et al.²⁸ observed that children with ADHD score poorly on clinical tests of blue color perception but not red-green. Moreso, when important on-screen information is displayed predominantly in blue-yellow colors in a virtual environment, children with ADHD tend to have poorer game experience than they do with red-green colors.²⁹

Primary open-angle glaucoma (POAG) and normal-tension glaucoma (NTG), also known as OAG, are a group of diseases characterized by progressive, irreversible degeneration of the retinal ganglion cells (RGCs) and their axons, causing a corresponding visual field (VF) loss with the observed signs of high and normal intraocular pressure, respectively. Studies done before now had indicated that VF defects may not be clinically detectable until 25 to 35% of all RGCs are lost. Acquired color vision deficiency in glaucoma was first described in 1883,³⁰ though blue-yellow deficiencies are generally associated with early glaucoma, while red-green deficiencies are generally associated with advanced glaucoma.³¹⁻³⁵

In this study, an effort was made to validate whether Dyop color testing could improve how color acuity is measured, to measure its reliability as to CA assessment, and also possibly to determine whether the measure of acuity in a range of colors would permit the development of a matrix of color perception to provide a rapid and precise diagnostic test for detection of dyslexia, ADHD, and changes in central visual function that correlate with the changes in the papillomacular structure of PPG and OAG subjects.

Methods

Research Design

This was a cross-sectional study. This research followed the tenets of the Declaration of Helsinki, and approval as well as ethical clearance was obtained from the ethical committee of Makkah Specialist Eye Hospital, Kano, Nigeria (Albasar International Foundation). Written informed consent was also obtained from all subjects. The research was conducted from August, 2021 to March, 2022.

Subjects

Normal subjects, patients with preperimetric glaucoma (PPG), patients with normal tension glaucoma (NTG), and patients with primary open-angle glaucoma (POAG) were recruited from Makkah Specialist Eye Hospital, Kano, and Bauchi, Nigeria.

Subjects diagnosed with dyslexia and ADHD by a seasoned neuropsychologist were recruited from the vision therapy clinic. The subjects included 23 eyes with POAG, 23 eyes with NTG, 22 eyes with PPG, 10 eyes with ADHD, 29 eyes with dyslexia, and 144 normal eyes (of which 22 subjects were used as a control group for glaucoma and PPG) that were not color blind and with unaided visual acuity of basic Dyop 8.0 arc minutes or better. Subjects included in glaucoma, PPG and control, and comparative study underwent an ophthalmological and general examination, which comprised the following: slit lamp and a funduscopy examination, gonioscopy, IOP measurement with Goldmann applanation tonometry, mean deviation (MD) measurement with SAP using the Swedish Interactive Threshold Algorithm (Standard 24-2) of the Humphrey Field Analyzer (Carl Zeiss Meditec Inc., Dublin, California), and qualitative color vision screening with Ishihara pseudoisochromatic plates and D15. Visual field measurements with fixation losses of more than 20% or with more than 33% are false positives or false negatives. MD was used for the evaluation of visual field function.

Subjects had reliable performance in visual field testing (fixation errors < 20%, false positives < 33%, and false negatives < 33%) and no cataract progression. The inclusion criteria for the normal eyes were visual acuity of basic Dyop 8.0 arc minutes or better, intraocular pressure (IOP) < 22 mmHg, normal findings on slit lamp and funduscopy examinations, and a visual field within the normal limits of the Anderson-Patella classification.³⁶ The inclusion criteria for the PPG eyes were best-corrected VA \geq 8.0; IOP < 22 mmHg without any treatment to lower IOP; a normal, open angle on a gonioscopic examination; glaucomatous changes in the optic disc, including neuroretinal rim thinning, notching, and cupping; and a visual field within the normal limits of a glaucoma hemifield test, with pattern standard deviation (PSD) greater than 5%, confirmed in at least two examinations. The inclusion criteria for glaucomatous (i.e., POAG and NTG) eyes were best-corrected VA of basic Dyop 8.00 arc minutes or better; glaucomatous changes in the optic disc; visual field defects conforming to the Anderson-Patella classification, confirmed in at least two visual field examinations; a normal, open angle on a gonioscopic examination; and IOP < 22 mmHg for POAG, < 12 mmHg for NTG if any treatments to lower IOP were used. Ongoing medical treatment, including IOP-lowering topical medication in patients with POAG and NTG, was not discontinued before the

examination. The inclusion criteria for dyslexia were verbal and non-verbal IQ within the normal range (> 85; based on the subtests of Block Design and Similarities of the Wechsler Intelligence Scale-IV for children)³⁷ and reading ability scores of at least 1.5 standard deviation (SD) below the normative mean on a sight-word efficiency test. The inclusion criteria for ADHD included fluency in English, normal body mass for age and gender, age of 8 to 23 years (inclusive), and a primary diagnosis of ADHD based on the Diagnostic and Statistical Manual of Mental Disorders - Fourth edition (DSM-IV) criteria.³⁸

The exclusion criteria for all subjects were: central visual field defects; clinical evidence or history of ocular disorders such as corneal, retinal and neural disease; presence of blood-flow-affecting systemic disease requiring medical treatment; concurrent stimulant use; any psychotic or neurologic condition, e.g., seizure disorder, bipolar disorder, and schizophrenia (not including ADHD and dyslexia); consumption of two or more standard alcoholic drinks per day; other drug abuse or extensive drug use; any experimental drug within the past four months (prior to the study); drug hypersensitivity or anaphylaxis; heavy caffeine use (more than four cups of coffee or equivalent per day); nicotine use; inability to comprehend and follow study procedures and instructions, based on the investigator's opinion; not prepared to sign the informed consent documents (including some with parents/guardians) prior to study entry; and refusal to agree to participation information and preparation requirements.

Color Acuity Measurements

In order to easily evaluate subjects' color vision performance with color acuity in a clinical setting, Dyop color test in Chart2020 version 12.0.1 computerized acuity unit was used. The Dyop color test shows a colored Dyop against an achromatic (neutral gray) background, calibrated for color accuracy. The luminance of the colored Dyop and the neutral gray background was uniform under various clinical lighting conditions. The chart was displayed to the subjects at 4 meters. The basic Dyop VA, refraction was corrected with a +2.00 lens, and +3.00 lens color (BOG, GOG, YOG, and ROG) acuity endpoints for normal eyes using Dyop Colors test were done. Visual acuity was taken with Dyop black/white-on-gray. The color acuity for ROG, GOG, BOG, and YOG was assessed for all subjects recruited into the six groups.¹³ The color acuity endpoints were recorded in arc minutes.

Collection and Statistical Analysis

This study was analyzed using Statistical Package for Social Science (SPSS) version 25.0, and the graphs were presented with Microsoft Excel version 2016. The data were presented as the mean \pm standard deviation. The Wilcoxon / Kruskal Wallis test (rank sums) with Bonferroni correction was used to determine the significant differences between groups in sex distribution. The Mann-Whitney U test with Bonferroni correction was used to determine the significant differences between groups in color acuity for distinct colors. The significance level was set at $p < 0.017$ in the Wilcoxon/Kruskal-Wallis test, Fisher's test, and Mann-Whitney U test. Finally, Spearman's rank correlation test was used to evaluate single correlations between MD and CVA for each color in glaucoma, PPG, and the control group. The significance level was set at $p < 0.05$ in the Spearman's rank correlation test.

Limitation of Study

The majority of the subjects did not tolerate a repetition of tests due to the number of tests conducted, and there was no other validated static or dynamic colored optotype to compare with the Dyop colors test as a method for a quantitative assessment of colors. Reliability was only measured by the limited variance within the specified CA groups.

Results

This prospective study investigated the clinical significance of CA in dyslexia, ADHD, PPG and OAG. A total of 251 eyes of 204 subjects (29 dyslexia eyes, 10 ADHD eyes, 22 PPG eyes, 23 NTG eyes, 23 POAG eyes, and 144 normal eyes as control group and for initial Dyop CA validation, aged 27.83 ± 14.44 years, (6–72 years)) were enrolled.

Dyop basic visual acuity (VA) and Dyop CAs were tested for BOG, GOG, YOG, and ROG in the various groups. Color acuity for BOG, GOG, YOG, and ROG was tested to investigate the pattern of CA in dyslexia, ADHD, PPG, POAG, NTG, and healthy normal eyes as controls.

A total of 50 eyes of 33 males and 17 females, with a mean age of 32.79 ± 8.59 years and 29.00 ± 6.61 years, respectively, were recruited, and another 47 subjects were tested bi-ocularly. Table 1 shows the validity of the Dyop colors test as to quantitative color acuity assessment of normal eyes. There was no significant difference as to gender and eye, but there was a significant difference in the quantitative and comparative assessment of basic Dyop and color

Table 1. Validity of Dyop Colors Test in Normal Eyes

Acuity Disparity for Normal Eye in arc minutes	Male (N = 33)	Female (N = 17)	P-value	Remark
Age (years)	32.79 ± 8.59	29.00 ± 6.61	0.27	NS (p > 0.05)
Black/White on Gray (BWG)	7.70* ± 0.59	8.00* ± 0.71	0.22	NS
Blue on Gray (BOG)	10.70* ± 2.20	11.71* ± 2.144	0.50	NS
Green on Gray (GOG)	9.18* ± 1.29	9.94* ± 1.63	0.17	NS
Yellow on Gray (YOG)	8.30* ± 0.95	8.88* ± 1.05	0.51	NS
Red on Gray (ROG)	10.61* ± 1.98	10.65* ± 1.90	0.94	NS
P-value	0.00	0.00		S
	Right Eye (N=47)	Left Eye (N = 47)	P-value	Remark
BOG	14.55* ± 5.52	14.11* ± 4.84	0.27	NS
GOG	13.32* ± 4.44	13.02* ± 3.98	0.18	NS
YOG	12.36* ± 3.70	12.06* ± 3.54	0.31	NS
ROG	14.47* ± 5.51	14.06* ± 4.54	0.09	NS
P-value	0.00	0.00		S

NS = Not Significant, S = Significant, * = Dyop arc minutes

Table 2. Reliability of Dyop Colors Test in Normal Eyes

Disparity For Increasing Blur in arc minutes	Baseline (N=16)	Baseline + 2D (N=16, p = 0.00)	Baseline + 3D (N=16, p = 0.00)
BOG	11.06* ± 2.72	18.19* ± 2.07	41.00* ± 15.08
GOG	8.94* ± 1.00	14.13* ± 1.54	23.06* ± 9.11
YOG	8.25* ± 1.13	12.44* ± 1.31	19.50* ± 6.11
ROG	10.44* ± 1.79	17.94* ± 2.91	37.00* ± 19.52
p-value	0.00	0.00	0.00

D = Diopter * = Dyop arc minutes

acuity of BWG, BOG, GOG, YOG, and ROG for male or female, as well as right or left eye.

Sixteen normotensive subjects were recruited to test the reliability of Dyop colors test. There was a significant difference in the quantitative and comparative assessment of basic Dyop and color acuity of BWG, BOG, GOG, YOG, and ROG in increasing blur with +2.00D and +3.00D for BOG, GOG, YOG, and ROG from baseline (Table 2). On the other hand, there was statistically significant Spearman correlation between BOG (r = 0.94, p = 0.00), GOG (r = 0.91, p = 0.00), YOG

(r = 0.93, p = 0.00), and ROG (r = 0.95, p = 0.00) with increasing diopters of blur (2.00D, 3.00D) (Figure 1). This suggests that a Dyop colors test is a reliable tool for quantitative colors assessment.

A total of 29 subjects aged 9.52 ± 2.32 years who were diagnosed with dyslexia were recruited and assessed bi-ocularly for the disparity in their basic Dyop visual acuity as well as Dyop colors. There was a significant difference in the basic Dyop visual acuity and YOG color acuity between right and left eyes, but there was no significant difference in color acuity assessment of BOG, GOG, and ROG bi-ocularly.

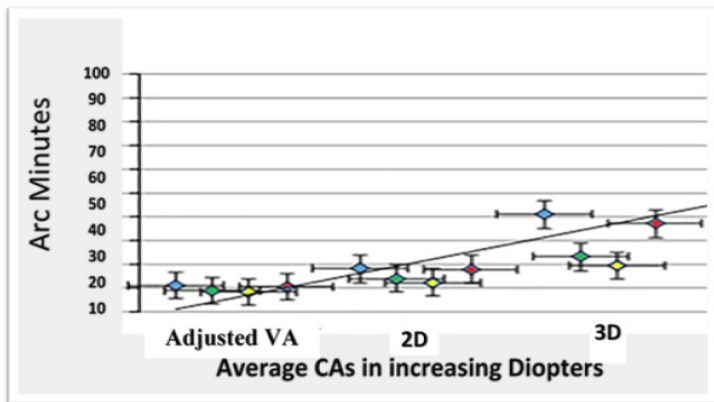


Figure 1. Reliability of Dyop Colors Test with Increasing Diopters of Blur

Table 3. Quantitative Dyop Colors Assessment for Dyslexics

Acuity Disparity for Dyslexia (N = 29, Age = 9.52 ± 2.32 years) in arc minutes	Right Eye	Left Eye	P-value
BWG	9.24* ± 2.42	8.52* ± 1.96	0.01
BOG	11.17* ± 2.74	11.10* ± 2.35	0.83
GOG	8.28* ± 1.96	8.03* ± 1.94	0.24
YOG	9.21* ± 2.23	8.52* ± 1.94	0.01
ROG	9.93* ± 2.73	9.59* ± 2.26	0.13

* = Dyop arc minutes.

Table 4. Quantitative Dyop Colors Assessment for ADHD

Acuity Disparity For ADHD (N=10, Age: 13.30 ± 4.74 years) in arc minutes	Right Eye	Left Eye	P-value
BWG	8.50* ± 0.97	8.60* ± 1.07	0.76
BOG	11.20* ± 1.55	12.10* ± 3.18	0.37
GOG	10.00* ± 1.56	9.90* ± 1.91	0.76
YOG	8.40* ± 1.00	8.60* ± 1.07	0.62
ROG	8.30* ± 0.67	8.30* ± 1.16	1.00

* = Dyop arc minutes

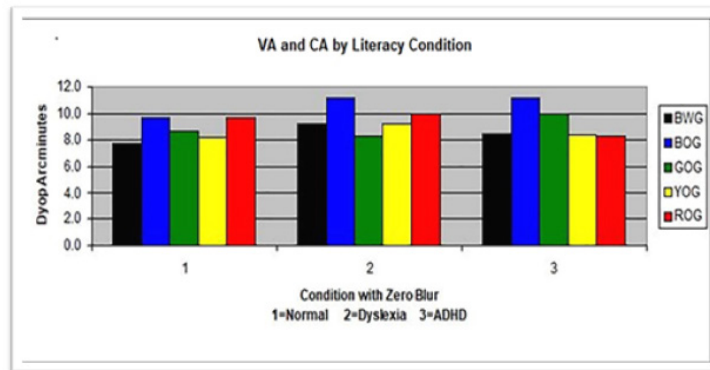


Figure 2. Comparative acuity in color pattern for possible literacy-associated conditions

Table 5. Characteristics of Normal, Open-angle, and Preperimetric Glaucoma

	Normal (N=22)	PPG (N=22)	POAG(N=23)	NTG (N=23)	Normal Vs PPG	Normal Vs NTG	PPG Vs NTG	NTG Vs POAG	Normal Vs POAG	PPG Vs POAG
	Mean ± SD				P-value					
Age (years)	29.05 ± 6.76	40.73±10.01	40.48±13.41	39.83 ±10.36	0.00	0.00	0.77	0.85	0.00	0.94
Sex (M:F)	13:9	20:2	21:2	9:14	0.12	0.19	0.00	0.00	0.01	0.96
IOP (mmHg)	16.95 ± 2.15	17.64 ± 1.79	18.70 ± 1.15	9.26 ± 0.86	0.26	0.00	0.00	0.00	0.00	0.02
CCT (µm)	557.36 ± 15.04	567.59 ± 17.31	536.96 ± 18.57	529.22 ± 19.62	0.17	0.04	0.00	0.18	0.00	0.00
MD (dB)	0.04 ± 0.18	-0.36 ± 0.77	-2.45 ± 5.83	-11.047 ± 5.88	0.02	0.00	0.00	0.42	0.00	0.00
PSD (dB)	1.54 ± 0.39	1.54 ± 0.68	11.41 ± 5.53	9.77 ± 5.78	0.97	0.00	0.00	0.33	0.00	0.00
Vessel density (%)	99.45 ± 0.51	85.41 ± 1.56	76.26 ± 4.78	76.17 ± 4.91	0.00	0.00	0.00	0.95	0.00	0.00
Avg RNFL (µm)	114.23 ± 7.14	92.95 ± 6.34	63.96 ± 3.72	65.87 ± 8.01	0.00	0.00	0.00	0.53	0.00	0.00
Avg GCC (µm)	97.81 ± 1.76	89.05 ± 6.24	59.70 ± 4.64	56.83 ± 9.32	0.00	0.00	0.00	0.19	0.00	0.00

PPG =preperimetric glaucoma, POAG =primary open angle glaucoma, NTG =normal tension glaucoma, IOP =intraocular pressure, CCT =central corneal thickness, MD =mean deviation, PSD =pattern standard deviation, RNFL =retinal nerve fibre layer, GCC =ganglion cell complex, Avg = Average, Sup = Superior, Inf = Inferior.

However, there was a significant difference in visual acuity, as well as colors acuity assessment, with best color acuity in GOG for the two eyes. (Table 3)

On the other hand, Table 4 shows a total of 10 subjects aged 13.30 ± 4.74 years who were diagnosed with ADHD were recruited and assessed bi-ocularly for the disparity in their basic Dyop visual acuity as well as Dyop colors. There was no significant difference in visual acuity as well as the colors acuity assessment when the two eyes were compared, but they were able to resolve the target best in red (i.e., ROG) monocularly and binocularly.

A total of 90 eyes of 90 subjects (22 normal eyes, 22 PPG eyes, 23 POAG eyes, and 23 NTG eyes aged 37.58 ±11.37 years (age range: 20–72 years)) were recruited. No patient failed color vision testing with the Ishihara pseudoisochromatic plates in both the glaucoma and control groups.

Table 5 shows the characteristics of the normal, PPG, and glaucoma eyes. The groups differed significantly as to IOP except for normal vs. PPG. There was no significant difference in PPG vs. NTG, NTG vs. POAG, and PPG vs. POAG assessment as to age; normal vs. PPG, normal vs. NTG, and PPG vs. POAG assessment as to gender; normal vs. PPG and NTG vs. POAG as to

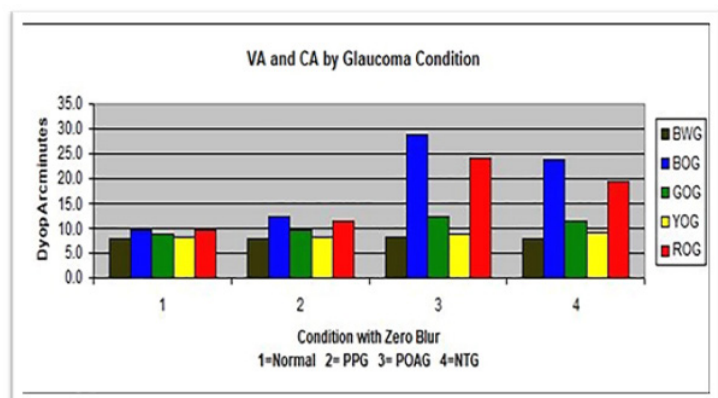


Figure 3. Comparative VA and CA pattern for glaucoma-associated conditions

Table 6. Quantitative Dyop Colors Assessment for Open-Angle Glaucoma, Preperimetric Glaucoma, and Normal

	Normal (22)	PPG (22)	POAG (23)	NTG (23)	Normal Vs PPG	Normal Vs NTG	PPG Vs NTG	NTG Vs POAG	Normal Vs POAG	PPG Vs POAG
	Mean ± SD				P-value					
BWG	7.77* ± 0.43	8.00* ± 0.00	8.13* ± 0.34	8.00* ± 0.00	0.01	0.02		0.08	0.00	0.08
BOG	9.68* ± 0.48	12.14* ± 1.58	28.87* ± 8.36	23.78* ± 9.24	0.00	0.00	0.00	0.60	0.00	0.00
GOG	8.68*	9.55* ± 0.91	12.17* ± 2.37	11.30* ± 2.24	0.00	0.00	0.00	0.21	0.00	0.00
YOG	8.18* ± 0.73	8.09* ± 0.29	8.70* ± 0.70	8.91* ± 1.81	0.59	0.09	0.04	0.59	0.02	0.00
ROG	9.68* ± 0.65	11.50*	24.35* ± 7.95	19.65* ± 6.29	0.00	0.00	0.00	0.03	0.00	0.00

* = Dyop arc minutes

Table 7. Association between Colors Acuity of POAG, NTG, Preperimetric Glaucoma, and Normal and Degree of Functional Loss

	Normal (N=22)			PPG (N=22)			NTG (N=23)			POAG (N=23)		
R, P-value	MD	RNFL	GCC	MD	RNFL	GCC	MD	RNFL	GCC	MD	RNFL	GCC
BOG	-0.03,0.89 ^c	0.00, 1.00 ^c	-0.09, 0.70 ^c	-0.04,0.86 ^c	-0.91, 0.00 ^c	-0.92, 0.00 ^c	-0.55,0.01 ^c	-0.60, 0.00 ^c	-0.57, 0.01 ^c	-0.47,0.02 ^c	-0.68, 0.00 ^c	-0.52, 0.01 ^c
GOG	-0.08,0.72 ^c	0.24, 0.28 ^c	0.05, 0.81 ^c	0.03,0.90 ^c	-0.67, 0.00 ^c	-0.70, 0.00 ^c	-0.21,0.35 ^c	-0.35, 0.10 ^c	-0.33, 0.12 ^c	-0.40,0.06 ^c	-0.29, 0.18 ^c	-0.13, 0.55 ^c
YOG	-0.20,0.38 ^c	-0.08, 0.73 ^c	0.18, 0.43 ^c	-0.16,0.47 ^c	-0.13, 0.58 ^c	-0.11, 0.62	-0.27,0.21	-0.47, 0.02 ^c	-0.44, 0.04 ^c	-0.36,0.09 ^c	-0.35, 0.11 ^c	-0.25, 0.25 ^c
ROG	0.23,0.30 ^c	-0.10, 0.67 ^c	0.22, 0.33 ^c	-0.13,0.56 ^c	-0.49, 0.02 ^c	-0.48, 0.02	-0.44,0.04 ^c	-0.44, 0.04 ^c	-0.42, 0.04 ^c	-0.43,0.04 ^c	-0.64, 0.00 ^c	-0.47, 0.02 ^c

R = Spearman correlation values, MD = mean deviation, RNFL = average retinal nerve fiber layer, GCC = ganglion cell complex, ^c = based on normal approximation

CCT assessment; NTG vs. POAG as to MD assessment; normal vs. PPG and NTG vs. POAG as to PSD assessment; NTG vs. POAG as to vessel density assessment; NTG vs. POAG as to average RNFL; NTG vs. POAG as to average GCC. However, there was a significant difference in other parameters comparing in between the groups.

There was no comparative assessment of PPG vs. NTG Dyop visual acuity (in arc minutes) because the standard deviation calculated is zero. Quantitative colors acuity was also measured in arc minutes, and the groups significantly differed in colors assessment. There was no significant difference in BOG assessment in NTG vs. POAG, but POAG assessment was worse in BOG color acuity than in NTG. In the same vein, there was no significant difference in NTG vs. POAG as to GOG color assessment. Normal vs. PPG and NTG vs. POAG were similar in their YOG color assessments, respectively. However, there was a significant difference in ROG color assessment for all groups, especially NTG vs. POAG; NTG eyes had a better ROG color acuity (NTG-ROG: 20 arc minutes or 20/100 and BOG: 24 arc minutes or 20/150; POAG-ROG: 24 arc minutes or 6/150 and BOG: 28 arc minutes or 20/200).

There was no association between the CA assessments for normal and the degree of functional loss. There was significant association between BOG, GOG, as well as ROG of PPG and the level of depletion of

RNFL as well as GCC. There was an association between decreased CA of blue as well as red in glaucoma (NTG and POAG), MD (BOG $r = -0.55$, $p = 0.01$; $r = -0.47$, $p = 0.02$; ROG $r = -0.44$, $p = 0.04$; $r = -0.43$, $p = 0.04$), RNFL (BOG $r = -0.60$, $p = 0.00$; $r = -0.68$, $p = 0.00$; ROG $r = -0.44$, $p = 0.04$; $r = -0.64$, $p = 0.00$), and GCC (BOG $r = 0.57$, $p = -0.01$; $r = -0.52$, $p = 0.01$; ROG $r = -0.42$, $p = 0.04$; $r = -0.47$, $p = 0.02$) findings.

Discussion

In this present study, interestingly, it was discovered that dyslexia and ADHD had best CA in GOG and ROG, respectively, while ROG and BOG were detectably impaired in eyes with NTG and POAG in very close association ($p < 0.05$) with a degree of functional loss, but GOG and YOG were not impaired in these eyes and not associated with glaucoma severity. However, there was a significant association ($p < 0.05$) between BOG, ROG, and GOG assessed in PPG and depletion of RNFL and GCC, which was not seen in control. Moreso, BOG acuity results worse than 20/50 for patients may be an indication of PPG, while BOG acuity results between 20/80 and 20/200 are markers for functional losses, usually sparing basic visual acuity (BWG). Hence, BOG acuity measurement is useful in the very early stage

of glaucoma, as well as in monitoring the progression of glaucomatous damage or functional losses. This suggests that measuring CA with the Dyop colors test may be a promising supplement to existing methods of detecting glaucoma, dyslexia, and ADHD, as well as evaluating the severity and/or management plan.

Validation and Reliability of the New Dyop Colors Test System

The most important components of human vision are spatial perception (comprising VA and contrast sensitivity), temporal perception (such as central critical fusion frequency), and color perception. The use of Dyop as a stimulus allows color spatial perception to be measured for each color in arc minutes. The CA comparison of the four colors was significantly different from the basic Dyop acuity irrespective of gender, eye, and increasing diopters (2D, 3D) of blur (Table 2). This validates the new Dyop colors test system as a promising tool for quantitative colors assessment.

However, there was a statistically significant association between BOG, GOG, YOG, and ROG ($p = 0.00$) with increasing diopters of blur. This suggests that a Dyop colors test is a reliable tool for quantitative color assessment.

Harris and Keim³⁹ investigated the accuracy of the Dyop acuity test with 162 participants by assessing the threshold acuities on a fully randomized basis, using Sloan letters and Dyop doublet with test conditions: uncorrected refraction and corrected refraction with +2.00 lens, +3.00 lens, +4.00 lens. There was a very strong linear Pearson correlation between Sloan and Dyop acuity measures for all of the test conditions for the subjects (Pearson $r = 0.95$; $p < 0.001$). The statistical variance in visual acuity measurement with the study condition revealed 0.193 and 0.035 for a projected Sloan and a Dyop doublet, respectively. The Dyop was found to be a novel method of measuring visual acuity that is strongly associated with and may offer an improvement in assessment of visual acuity compared to Sloan letters. The Dyop was also reported to be advantageous due to the speed at which the threshold acuity endpoint is defined, finer acuity granularity as compared to the typically used acuity "line" steps, and ease of endpoint identification by subjects. The 2015 Dyop doublet was also found to be simpler to use, easier in eliminating unreliable responses, and less variable than the prototype 2013 Dyop triplet. The linear increase in Dyop acuity endpoint angular diameter with increase in blur for the 2015 Dyop doublet was also smaller than the prototype 2013 Dyop triplet. The linearity of the Dyop angular width with

increased blur, versus the classical Snellen logarithmic increase, is likely due to the Dyop having a smaller gap/segment area of 0.54 arc minutes squared versus the averaged (theoretical) Snellen gap/stimulus area of 1.00 arc minute squared. The logarithmic disparity directly correlates to the Snellen gap being twice the actual and empirically measured gap of the Dyop test, as well as contributing to the higher variance of the Snellen test to the variance of the Dyop test.

Moreso, the Dyop color test system consists of a personal computer with a color-calibrated, high-accuracy LCD display, allowing the stimulus and background to have equivalent luminance. Older tests, such as the Ishihara color test, standard pseudoisochromatic plates, and the Farnsworth Dichotomous Test Panel D-15, can provide various values, but these values represent fundamentally different properties of vision (qualitative measure) rather than CA (quantitative), which is what drives our interest here. Moreso, these tests require a significant amount of time, and they are a paper-based approach, which has been relatively limited in its ability to reproduce colors precisely. An initial comparison of Dyop colors perception and dyslexia diagnosis done by Stark¹⁰ in younger and older subjects showed the benefits of this system. In the present study, based on the previous work, CAs in dyslexia, ADHD, glaucoma, PPG, and normal eyes were evaluated. In the same vein, the Dyop colors test eliminates differences in the chromatic intensity of the stimulus and background.

Color Vision and Dyslexia

This current study showed that CA for green was detectably better than yellow, red, and blue in the eyes diagnosed with dyslexia. This finding points to the effect of color text and/or colored filters on enhanced performance in dyslexic children (Figure 2).

Studies have shown that reading performance was improved in yellow and blue filter conditions,^{40,41} and Razuk et al.⁴² also suggested that the green filter improves reading performance in children with dyslexia because the filter most likely facilitated cortical activity and decreased visual distortions. However, there is another study by Henderson et al.⁴³ that revealed that the use of colored filters during reading in undergraduate students with and without dyslexia improved reading rate, but the dyslexics showed marginally larger gains in reading rate with the filters on than their non-dyslexic peers did. Contrarily, Denton and Meindl⁴⁴ did not find any significant improvements in reading from the use of

colored filters in three individuals with dyslexia aged 7, 11, and 32 years old.

Color Vision and ADHD

This current study showed that CA for red was detectably better than yellow, green, and blue in the eyes diagnosed with ADHD. These findings suggest that red color tests and/or red colored filters may best enhance performance in people with ADHD (Figure 2).

Several studies revealed reduced speed in color processing in ADHD population.⁴⁵ Notably, the “retinal dopaminergic” hypothesis of color vision⁴⁶ opines that a deficiency in central nervous system (CNS) dopamine in ADHD may induce a hypo-dopaminergic tone in the retina, which consequently would have depleting effects on short-wavelength (“blue”) cones. Blue cones are very sensitive to dopamine (as well as other neurochemical agents) and are relatively scarce in number, so the purportedly low dopaminergic tone in ADHD⁴⁷ may cause the reduced blue-yellow color perception.

Studies on color discrimination in children with ADHD point to perceptual problems, especially for the blue-yellow axis, but the red-green axis also appears to be affected. In line with the finding of impaired blue-yellow color discrimination in ADHD is a study that found that in contrast to red-green stimuli, blue-yellow stimuli resulted in decreased performance of participants with ADHD in virtual reality computer games.⁴⁸ However, Banaschewski et al.⁴⁹ also investigated color perception in children with ADHD, as well as the relationship between color perception and performance on a conventional neuropsychological task (Stroop task) that requires timed naming of colored stimuli in children, and the findings indicated subtle problems in the blue-yellow mechanism and changes in retinal dopaminergic mechanisms in children with ADHD; the deficit was accounted for correspondingly by blue-yellow and red-green discrimination abilities. Results for color discrimination in adults with ADHD are inconsistent, with one study finding decreased discrimination for the blue spectrum only, while another study could not reveal any differences between ADHD and normal. Perhaps color discrimination is differentially affected in children and adults with ADHD, and adults may have developed compensation strategies to account for their perceptual problems in color discrimination.²⁷ However, in this current study, our interest is in the color acuity of children with ADHD, and the findings seem to be consistent with some of the previous studies on the color perception of children with ADHD.

Acquired Color Vision Defects and Glaucoma

Acquired color vision deficiency in glaucoma was first described in 1883,⁵⁰ though blue-yellow deficiencies are generally associated with early glaucoma, while red-green deficiencies are generally associated with advanced glaucoma.⁵¹⁻⁵⁵ Cone cells are categorized into three types—L-, M-, and S-cones—based on their pigment. The L-cones being the most common account for more than 50%, next is the M-cones, with a very minor proportion being S-cones, at less than 10% of the cone cells.⁵⁶ However, the S-cone is said to be highly vulnerable to damage,⁵⁷ which perhaps may lead to debatably acquired blue-yellow color vision deficiency. Consequently, S-cone impairment occurs before L- and M-cone impairment in glaucoma. However, the L-cones (red), and M-cones (green) are preferentially affected by glaucoma in experimental models of glaucoma.⁵⁸ Such studies concentrated on patients with advanced retinal disease, and it is now generally accepted that glaucoma first causes an acquired S-cone mechanism deficiency on conventional color vision tests such as the F-M 100-Hue and desaturated D15.⁵⁹ The current study also showed that Dyop CA in blue and red was detectably lower in eyes with glaucoma than in PPG and healthy eyes. These current results also revealed that the blue CA is more affected than the red in NTG and POAG (Figure 3). This suggests that glaucoma is a cause of acquired color vision defects. The main sign of glaucoma is elevated IOP, which affects the cone cells,⁶⁰⁻⁶³ but routine color acuity assessment of glaucomatous eyes and suspects will potentiate our ability to detect and/or monitor these irreversible functional losses due to glaucoma.

Moreso, there was an association between decreased CA of blue as well as red in glaucoma (NTG and POAG), MD; BOG, and ROG, RNFL; BOG, and ROG as well as GCC; BOG, and ROG ($p < 0.0$). This suggests that the functional loss due to depletion of VF, RNFL, and macula thickness is in association with glaucoma progression (either normal-tension or high-tension glaucoma). Furthermore, there is association between reduced CA for blue, red, and green and depletion of RNFL and GCC findings for PPG, but blue has the highest association (91% and 92%, respectively), which suggests that suspicious cupping of the optic disc with reduced blue CA of 12 arc minutes (6/14) or worse with no VF defect may be diagnostic for PPG.

Ouchi et al.⁶⁴ also investigated the clinical significance of color visual acuity (CVA) in PPG and OAG, with a total of 123 eyes of 73 subjects (22 normal

eyes, 14 PPG eyes, and 87 OAG eyes; mean age: 44.9 ± 10.1 years, age range: 21-64 years) enrolled. CVA was tested for red, green-yellow, blue-green, and blue-purple with a newly developed test. Red VA and blue-green VA were significantly worse in the OAG eyes than in the normal eyes ($p = 0.008$ and $p = 0.015$, respectively), although green-yellow VA and blue-purple VA were not significantly worse. Furthermore, red VA and blue-green VA were significantly correlated with MD in a group of eyes with either PPG or OAG ($r = -0.23$, $p = 0.023$; $r = -0.25$, $p = 0.012$, respectively), but green-yellow VA and blue-purple VA were not. In this current study, samples were taken for NTG and POAG to make up OAG.

Niwa et al.³⁶ evaluated acquired color vision deficiency in glaucoma by using the Rabin cone contrast test (RCCT) with 27 eyes of 27 patients with glaucoma (glaucoma group) and 27 eyes of 27 normal subjects (control group). Long (L), medium (M), and short (S) CCT scores were measured. The Humphrey automated perimetry was analyzed using the Swedish Interactive Thresholding Algorithm 30-2, and the mean deviation (MD) was evaluated. The GCIPL thickness was measured using high-definition OCT in the glaucoma group. The mean M CCTs and S CCTs in the glaucoma group were significantly lower ($p < 0.05$ for both comparisons) than in the control group (M CCTs, 80.7 ± 16.8 vs 91.9 ± 8.22 ; S CCTs, 83.9 ± 19.5 vs 97.4 ± 3.77 , respectively); the L CCTs did not differ significantly ($p = 0.065$) from those of the controls (91.8 ± 12.8 vs 97.4 ± 3.50 , respectively). The M CCTs and S CCTs were correlated significantly with those of MD (M CCTs, $r = 0.47$; S CCTs, $r = 0.44$; $p < 0.05$ for both comparisons) and GCIPL thickness (M CCTs, $r = 0.70$; $p < 0.0001$; S CCTs, $r = 0.57$; $p < 0.01$). In this current study, Dyop colors test system with a rotating colored optotype that resonates with the refresh rate of the photoreceptors was used to measure the CAs.

Kim et al.⁶⁵ investigated the topographic relationship between macular superficial microvessel density (SMD) and macular ganglion cell-inner plexiform layer (GCIPL) thickness in eyes; 25 eyes of 25 patients with PPG and 86 eyes of 86 patients with early NTG. A customized software program was used to analyze the macular SMD from the optical coherence tomography angiography (OCTA) and scan images of all subjects. Macular GCIPL thickness showed significant correlations with macular SMD in the superotemporal (ST), inferotemporal (IT), and inferoinferior (II) sectors in PPG and patients with early NTG ($r = 0.191$, 0.373 and 0.346 for ST, IT and II sector, respectively).

The circumpapillary retinal nerve fiber layer (RNFL) thickness and macular SMD also showed significant correlations between the ST sector of the macula and the 1, 9 clock-hour peripapillary regions and between the IT and II sectors of the macula and the 6, 7, 8 clock-hour peripapillary regions. In this current study, average RNFL thickness and average GCC were used to correlate the CA assessments.

Glaucoma Progression

The use of CA as a method of detecting glaucoma and monitoring its progression is a major focus of this current study and could be the most promising as to technological advancements in detecting glaucoma and evaluating its severity. Blue-on-yellow perimetry has been the standard for early detection of glaucoma,⁶⁶ and frequency doubling technology perimetry has also been reported to be effective in detecting early glaucomatous losses.^{67,68} OCT measurement of cpRNFLT captures presence of glaucoma, and cpRNFLT depletes with the severity of glaucoma.⁶⁹⁻⁷² Macular ganglion cell complex thickness measurements have also been reported accurately to estimate glaucoma progression, similar to cpRNFLT findings, even in eyes with high myopia.^{73,74} Glaucomatous changes and visual field constriction is equally detectable by new perimetric techniques that enhance glaucoma progression assessment.^{75,76} Meanwhile, other research considered optic nerve head blood flow impairment, which may also be involved in glaucoma progression.⁷⁷

Conclusion

In conclusion, this study investigated the validity, reliability, and use of Dyop colors test to measure the changes in CA in dyslexia, ADHD, PPG, NTG, and POAG. It was discovered that green and red CAs were detectably best in dyslexics and ADHD, respectively; blue and red were detectably worse in eyes with glaucomatous optic neuropathy, in close association with the degree of functional loss. However, green and yellow CAs were not impaired in eyes with glaucoma, and there was no association with glaucoma severity. These findings suggest that measuring the various types of CA with the new Dyop colors test described in this study may be a very efficient supplement to the existing methods of detecting dyslexia, ADHD, and glaucoma, as well as evaluating the severity of these diseases.

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