Influence of learning effect on blue-on-yellow perimetry

Y. ZHONG, L. CHEN, Y. CHENG, P. HUANG

Department of Ophthalmology, Ruijin Hospital Affiliated Shanghai Jiaotong University, Shanghai - China

PURPOSE. *Some studies have found that a significant blue-on-yellow perimetry (B/YP) learning effect exists in patients with ocular hypertension (OHT) or open-angle glaucoma who were experienced in standard automated perimetry. However, very little is known about the B/YP learning effect in normal subjects and patients without previous white-on-white perimetry (W/WP) experience. Meanwhile, it is unclear whether the B/YP learning effect is influenced by age and refraction.*
METHODS. *Twenty healthy subjects, 26 OHT and 14 primary open angle glaucoma (POAG) patients, underwent three full-threshold B/YP tests at intervals of 7 to 21 days. Of the 60 subjects, 38 had no previous W/WP experiences, 22 had previous W/WP experiences for at least two times. The parameters investigated to detect a learning effect were the perimetric indices and the test duration (TD).*
RESULTS. *Learning effects were demonstrated for mean deviation (MD), pattern standard deviation (PSD), short-term fluctuation (SF), and TD. Significant differences were found between the MD, PSD, SF, and TD of the first test and those of the second and third tests (p<0.05). However, no difference was found between those parameters of the second and third tests. No statistically significant differences were noted in terms of $MD_{1st-2nd}$, $MD1_{st-3rd}$, $PSD_{1st-2nd}$, $PSD_{1st-3rd}$, $TD_{1st-2nd}$, and $TD_{1st-3rd}$ between the group with W/WP experience and the group without previous W/WP experience (p>0.05). No statistically significant differences were noted in terms of those parameters among the normal subjects and the patients with OHT or POAG (p>0.05). No significant difference was found in the B/YP learning effect among various age groups (p>0.05) and among various refraction groups (p>0.05).*
CONCLUSIONS. *A significant learning effect was observed between the first and the second or third tests and the perimetric indices appeared improved at full-threshold B/YP. The previous W/WP experience and the subject age and refraction did not influence the B/YP learning effect. This above all should be taken into account when considering the clinical use of this test to avoid erroneous diagnostic conclusions. (Eur J Ophthalmol 2008; 18: 392-9)*

KEY WORDS. *Blue-on-yellow perimetry, Learning effect, Normal subject, Ocular hypertension, Primary open angle glaucoma*

INTRODUCTION

Since Pederson and Anderson (1) and Quigley and associates (2) showed that, with white-on-white perimetry (W/WP), early glaucomatous visual field damage may not be detected until 30% of the ganglion cells are lost, several psychophysical tests have been developed to detect early glaucomatous damage, including frequency-doubling technology (FDT), high-pass perimetry, motion automated perimetry, flicker perimetry, and blue-on-yellow perimetry (B/YP) (3-13).
B/YP is a type of visual field examination technique which

is a combined method of visual field test and color vision test. B/YP is considered to be able to detect the defect of short-wavelength color visual fields (14). Research has shown that the B/YP is a high sensitivity method for detecting visual field defects and predicting the development of visual field loss in glaucoma (12, 13, 15, 16).

In W/WP or standard threshold perimetry, the learning effect can influence the results of a visual field test in both healthy and glaucomatous patients (17-20). Healthy untrained subjects tend to produce specific patterns of artifactual field loss, which in glaucomatous patients are added to the truly pathologic perimetry defects (21, 22). Thus, patients need time to learn any new psychophysical test and tend to improve their performance in subsequent examinations (22).

The B/YP learning effect has been reported by others (23, 24). Rossetti et al (23) and Wild et al (24) found that a significant B/YP learning effect existed in patients with ocular hypertension (OHT) or open-angle glaucoma who were experienced in standard automated perimetry. However, very little is known about the B/YP learning effect in normal subjects and patients without previous W/WP experience. Meanwhile, it is unclear whether the B/YP learning effect is influenced by age and refraction. The purpose of our study is to evaluate the influence of learning effect on B/YP in healthy subjects and patients with OHT and primary open angle glaucoma (POAG) with or without previous W/WP experience, and to investigate the influence of age and refraction on the B/YP learning effect.

METHODS

The research followed the tenets of the Declaration of Helsinki and all subjects signed an informed consent before inclusion in the study.

Twenty healthy subjects, 26 patients with OHT, and 14 patients with POAG were recruited from the Ophthalmology Department of Ruijin Hospital, and one eye each was randomly chosen from those subjects for inclusion in this study. No subject had been evaluated by B/YP before. Subjects were not excluded on the basis of gender, age, or race. Color blindness and other eye diseases and neurologic diseases were excluded for all subjects. The mean age of healthy subjects, patients with OHT, and patients with POAG was 43.10±14.59 years (range 25–69), 47.31±11.81 years (range 21–61),

and 53.71±10.20 years (range 46–73). In the healthy subjects group, 10 of the 20 subjects were men, in OHT group, 6 of the 26 patients were men, and in POAG group, 6 of the 14 patients were men. The refractive error ranged from –7 to +5 diopters. All patients had a corrected visual acuity equal to or better than 0.8. Of the 60 subjects, 38 had no previous W/WP experiences (including 20 normal subjects and 18 OHT), 22 had previous W/WP experiences for at least two times (including 8 OHT and 14 POAG).

The inclusion criteria for healthy subjects were corrected visual acuity ≥0.8, refractive error ranging between +5 and –7 spherical diopters, intraocular pressure (IOP) <21 mmHg, absence of optic disc abnormalities (such as cup/disc ratio >0.5, localized defect in the neuroretinal rim, nasal cupping, disc hemorrhage, or cup/disc asymmetry >0.2), and normal results in W/WP (less than three adjacent points within p<5% at the corrected probability plot). Subjects with lens or corneal opacities, any abnormality in the retina (such as age-related macular degeneration, diabetic retinopathy, vein occlusion), glaucoma in the other eye, previous ocular surgery, family history of glaucoma, migraine, or neurologic disease were excluded. Patients with OHT were identified if they had high IOP measured by Goldmann applanation tonometer (IOP >21 mmHg without any treatment), normal visual field with conventional W/WP, open angle at gonioscopy, and normal optic nerve head and retinal nerve fiber layer on clinical examination (25).

Patients were classified as having POAG when they had a typical glaucomatous visual field with conventional W/WP and/or a typical abnormal optic nerve head, open angle at gonioscopy, IOP >21 mmHg with no treatment, and no clinically apparent secondary cause for their glaucoma (25). A glaucomatous visual field defect was defined as follows: three adjacent points depressed by 5 dB, with one of the points depressed by at least 10 dB; two adjacent points depressed by 10 dB; or a 10 dB difference across the nasal horizontal meridian in two adjacent points.

None of the points could be edge points unless immediately above or below the nasal horizontal meridian (26, 27). In addition, the results adopted for a reliable test were less than 20% of fixation loss, 20% of false-positive, and 33% of false-negative. The optic nerve head was examined by two glaucoma specialists (Y.Z., Y.C.), and the abnormal optic nerve head classification was based on the presence of an optic rim notch or of dif-

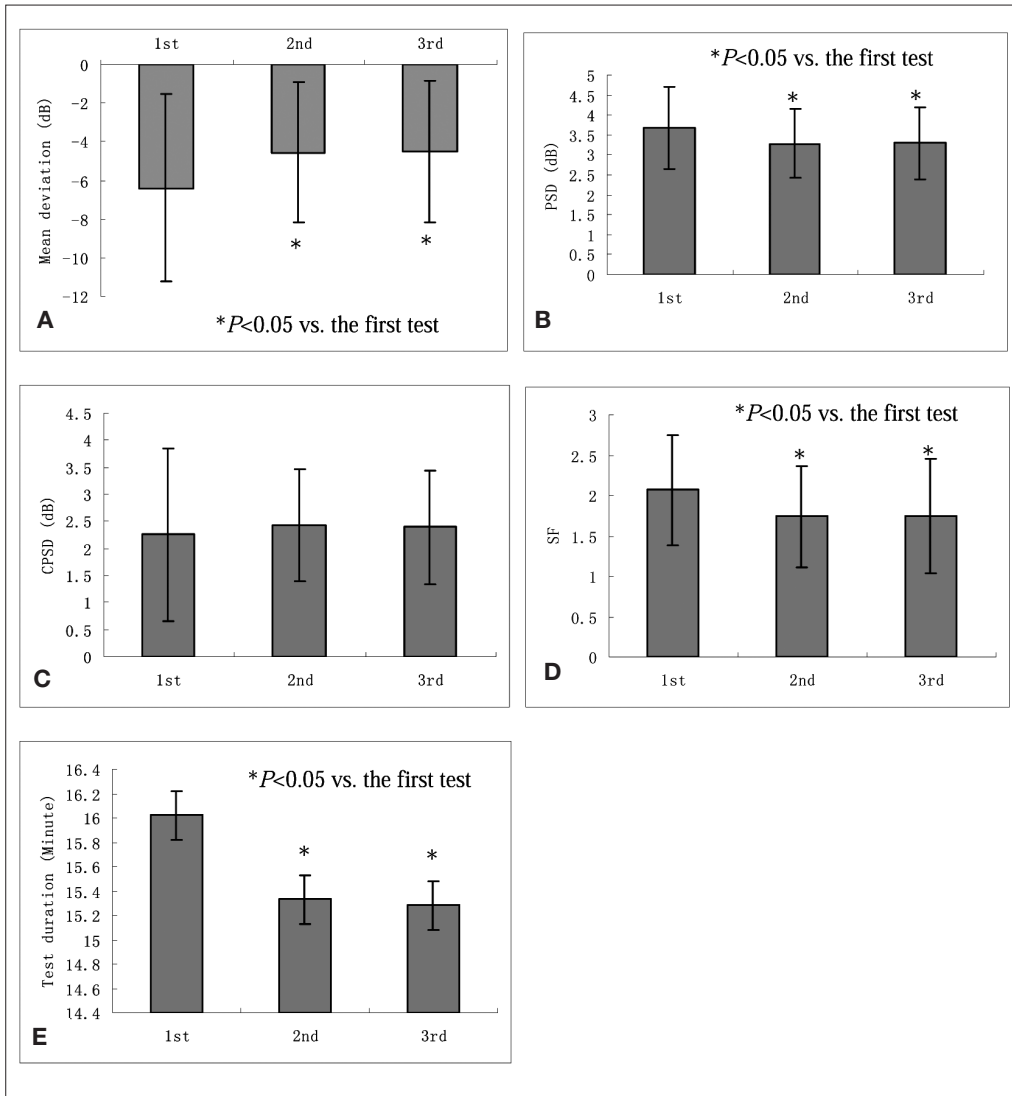*Influence of learning effect on blue-on-yellow perimetry*

Fig. 1 - *Results of mean deviation (MD), pattern standard deviation (PSD), corrected pattern standard deviation (CPSD), short-term fluctuation (SF), and test duration (TD) shown among three blue-on-yellow perimetry (B/YP) tests.* **(A)** *The differences between first and second, first and third results with regard to MD were significant (p=0.004 and p=0.0038, respectively).* **(B)** *The differences between first and second, first and third results with regard to PSD were significant (p=0.016 and p=0.028, respectively).* **(C)** *No significant differences of CPSD were noted among three B/YP tests (p>0.05).* **(D)** *The differences between first and second, first and third results with regard to SF were significant (p=0.002 and p=0.0017, respectively).* **(E)** *The differences between first and second, first and third results with regard to TD were significant (p=0.021 and p=0.019, respectively).*

fuse/generalized loss of optic rim tissue, vertical cup/disc (C/D) diameter ratio asymmetry unexplained by side differences in optic disc size, and disc hemorrhage. All subjects' visual fields were assessed by Humphrey field analyzer 750i (Carl Zeiss Meditec, Dublin, CA, USA), program 30-2, full threshold. The test parameters for B/YP were as follows: the yellow background luminance was 89 candela/m^2, Goldmann size V blue stimulus was used for the stimulus target, and the target duration time was 200 milliseconds and the interval time was 600 milliseconds. The crosshair in the screen provided a central fixation mark. Data analysis was derived from all 76 single data points in the central 30 degrees of the visual field. All patients had a background illumination adaptation for 5 to 10 minutes before visual field exami-

nation. All visual field examinations were performed under the natural pupil size. If there was presbyopia present, it was corrected by using proper convex lenses. In order to make the patient understand the test procedure, one eye of each patient was randomly selected to undergo about 1 minute training session before actual test. The results of this training session were discarded. Right eye was tested first, and then left eye with 30 minutes break. The test results were stored and printed. The criteria of abnormal B/YP were the same as those of W/WP (12, 25).
All subjects had three B/YP tests, and the interval between the tests was at least 7 days and maximally 21 days in order to avoid the effect of the progress of the visual field loss. Mean deviation (MD), pattern standard deviation (PSD), corrected pattern standard deviation

Fig. 2 - *The differences of mean deviation (MD), pattern standard deviation (PSD), and test duration (TD) between the first and the second blue-on-yellow perimetry (B/YP) tests, between the first and the third B/YP tests.* **(A)** *No statistically significant differences were noted in terms of the MD$_{1st-2nd}$ and MD$_{1st-3rd}$ between the group with white-on-white perimetry (W/WP) experience and the group without previous W/WP experience (p=0.362 and 0.451, respectively).* **(B)** *No statistically significant differences were noted in terms of the PSD$_{1st-2nd}$ and PSD$_{1st-3rd}$ between the group with W/WP experience and the group without previous W/WP experience (p=0.705 and 0.648, respectively).* **(C)** *No statistically significant differences were noted in terms of the TD$_{1st-2nd}$ and TD$_{1st-3rd}$ between the group with W/WP experience and the group without previous W/WP experience (p=0.318 and 0.589, respectively).*
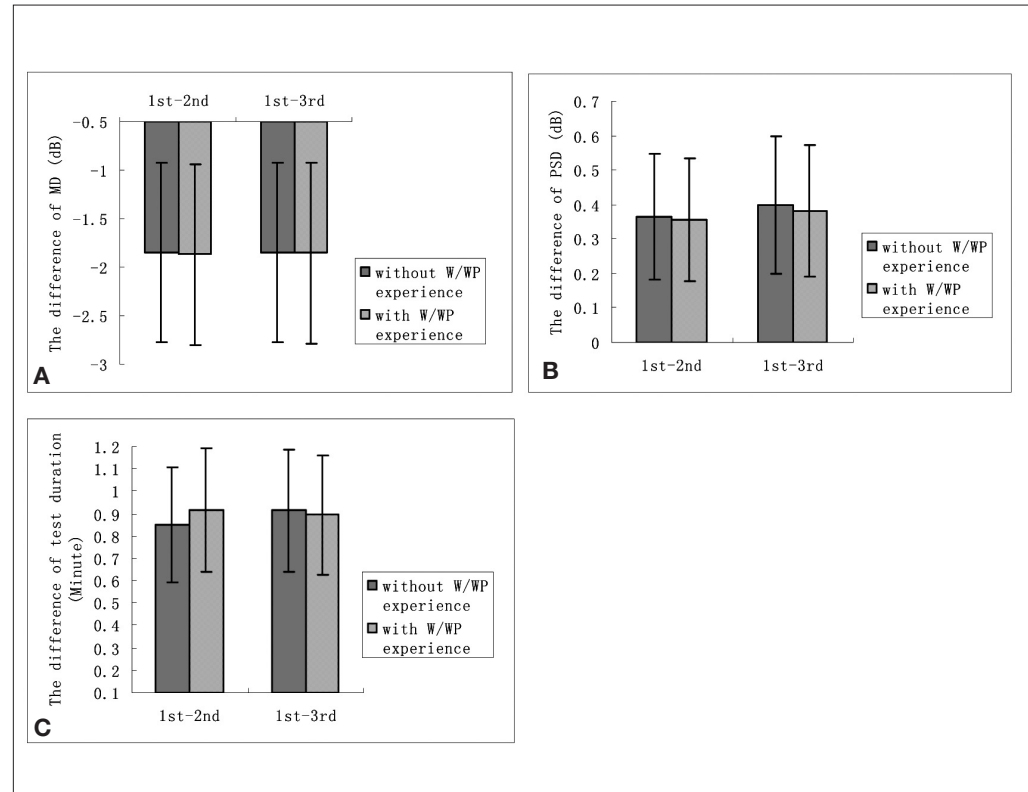
(CPSD), short-term fluctuation (SF), and the test duration (TD) were considered in the study.

Data are expressed as mean ± SD, unless otherwise stated. Statistical analysis was performed with the SPSS program (version 12.0, SPSS Inc., 2003). The Kolmogorov-Smirnov test was used to evaluate whether the samples were normally distributed. Because the distribution of the MD, PSD, and TD was normal, one-way analysis of variance (ANOVA) followed by the Scheffe test (homogeneity of variance) or Games-Howell test (non homogeneity of variance) was used for comparing the data among the first, the second, and the third tests. Because the distribution of the CPSD and SF was not normal and the data were paired, the Wilcoxon matched-paired test was used for statistical analysis. p<0.05 Was considered to be statistically significant.

RESULTS

Compared with the first test, 51 of the 60 tested subjects had an improvement in B/YP results, and 9 subjects showed unchanged or slightly deteriorated B/YP results.

For all the tested subjects, the MD in the first, second, and third B/YP tests were –6.40±4.86 dB, –4.55±3.61 dB, and –4.51±3.70 dB, respectively. When the MD measured in all subjects during the three B/YP tests were compared, significant differences were found between the MD of the first test and that of the second (p=0.004) and third (p=0.0038) tests. No difference was found between the MD of the second and third tests (Fig. 1A). The PSD was 3.68±1.03 dB at the first, 3.29±0.88 dB at the second, and 3.30±0.91 dB at the third B/YP tests. Significant differences were noted between the first and second (p=0.016) and the first and the third (p=0.028) tests, but no difference was found between the PSD of the second and third tests (Fig. 1B). Figure 1C shows the CPSD in the three B/YP tests; there were no significant differences of the CPSD values among the three tests (p>0.05). The SF in the first, second, and third B/YP tests were 2.07±0.68, 1.74±0.63, and 1.73±0.71, respectively. Significant differences were found between the first and second (p=0.002) and the first and the third (p=0.0017) tests, but no difference was found between the SF of the second and third tests (Fig. 1D). The TD was 16.02±1.73 minutes at the first, 15.33±1.53 minutes at the second, and 15.28±1.60
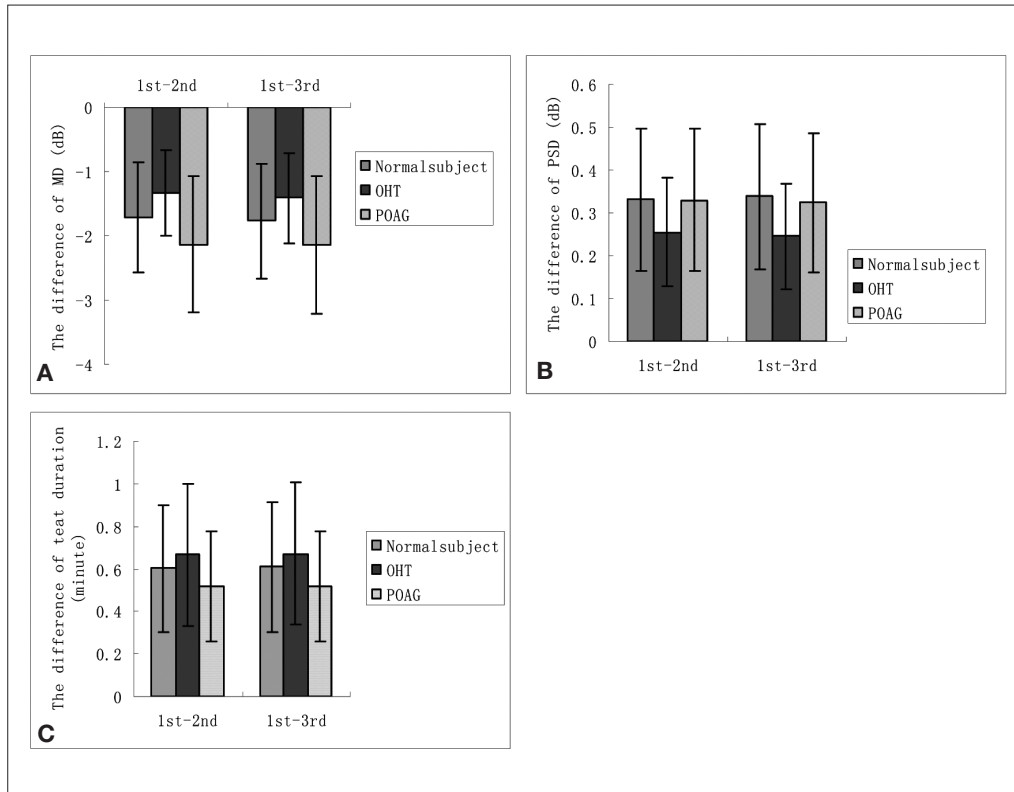
Fig. 3 - *The differences of mean deviation (MD), pattern standard deviation (PSD), and test duration (TD) between the first and the second blue-on-yellow perimetry (B/YP) tests, between the first and the third B/YP tests.* **(A)** *No statistically significant differences were noted in terms of the $MD_{1st-2nd}$ and $MD_{1st-3rd}$ among the normal subject, ocular hypertension (OHT), and primary open angle glaucoma (POAG) groups (p=0.614 and 0.682, respectively).* **(B)** *No statistically significant differences were noted in terms of the $PSD_{1st-2nd}$ and $PSD_{1st-3rd}$ among the normal subject, OHT, and POAG groups (p=0.953 and 0.741, respectively).* **(C)** *No statistically significant differences were noted in terms of the $TD_{1st-2nd}$ and $TD_{1st-3rd}$ among the normal subject, OHT, and POAG groups (p=0.880 and 0.858, respectively).*
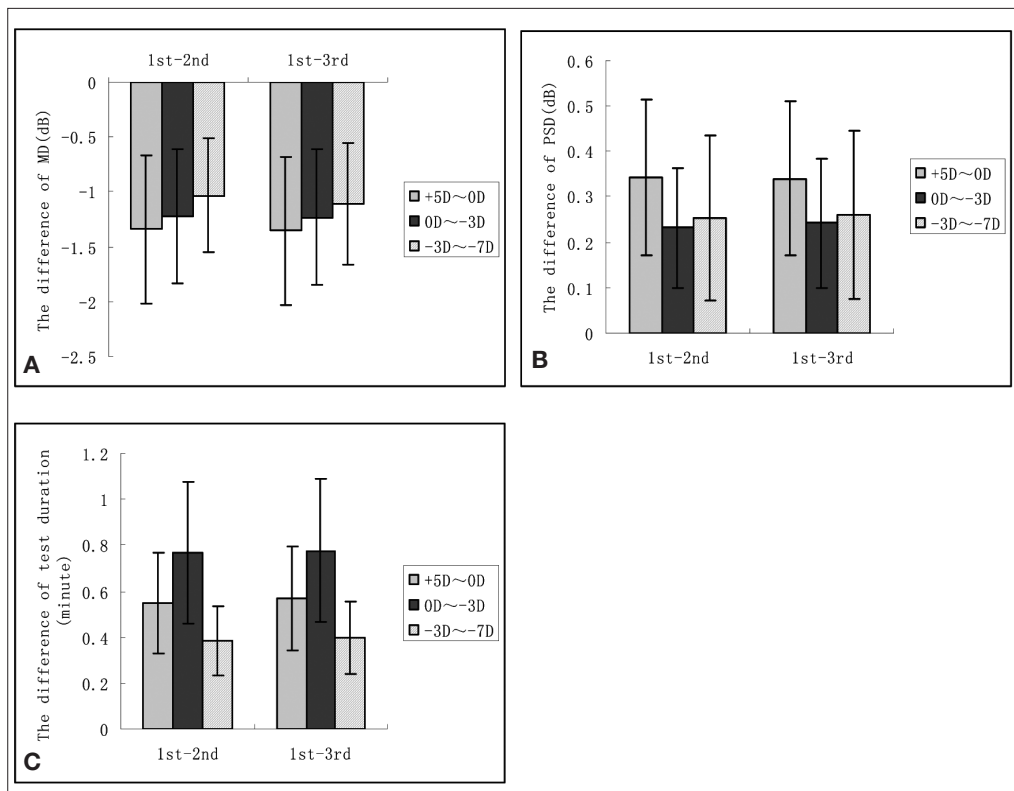

Fig. 4 - *The differences of mean deviation (MD), pattern standard deviation (PSD), and test duration (TD) between the first and the second blue-on-yellow perimetry (B/YP) tests, between the first and the third B/YP tests.* **(A)** *No statistically significant differences were noted in terms of the $MD_{1st-2nd}$ and $MD_{1st-3rd}$ among the +5 D~0 D, 0 D~–3 D, and –3 D~–7 D groups (p=0.977 and 0.962, respectively).* **(B)** *No statistically significant differences were noted in terms of the $PSD_{1st-2nd}$ and $PSD_{1st-3rd}$ among the +5 D~0 D, 0 D~–3 D, and –3 D~–7 D groups (p=0.597 and 0.603, respectively).* **(C)** *No statistically significant differences were noted in terms of the $TD_{1st-2nd}$ and $TD_{1st-3rd}$ among the +5 D~0 D, 0 D~–3 D, and –3 D~–7 D groups (p=0.084 and 0.088, respectively).*

Fig. 5 - *The differences of mean deviation (MD), pattern standard deviation (PSD), and test duration (TD) between the first and the second blue-on-yellow perimetry (B/YP) tests, between the first and the third B/YP tests.* **(A)** *No statistically significant differences were noted in terms of the* $MD_{1st\text{-}2nd}$ *and* $MD_{1st\text{-}3rd}$ *among the 20~40 years, 40~60 years, and more than 60 years groups (p=0.277 and 0.380, respectively).* **(B)** *No statistically significant differences were noted in terms of the* $PSD_{1st\text{-}2nd}$ *and* $PSD_{1st\text{-}3rd}$ *among the 20~40 years, 40~60 years, and more than 60 years groups (p=0.292 and 0.469, respectively).* **(C)** *No statistically significant differences were noted in terms of the* $TD_{1st\text{-}2nd}$ *and* $TD_{1st\text{-}3rd}$ *among the 20~40 years, 40~60 years, and more than 60 years groups (p=0.651 and 0.694, respectively).*
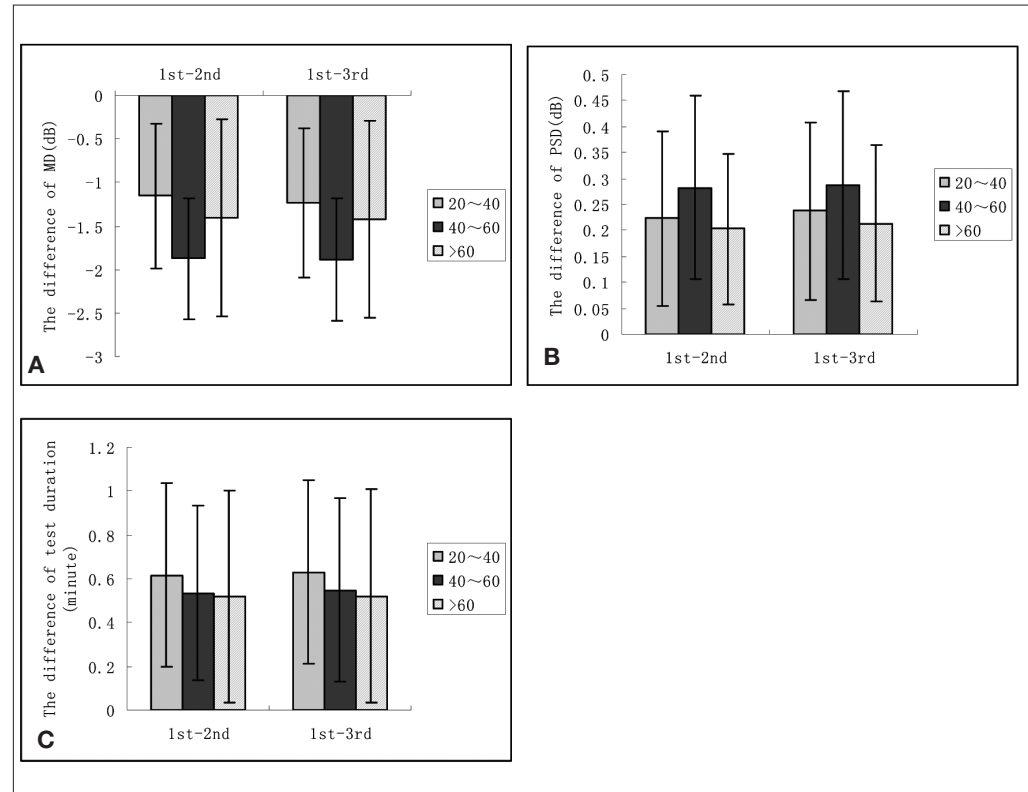
minutes at the third B/YP test. Significant differences were noted between the first and second (p=0.021) and the first and the third (p=0.019) tests, but no difference was found between the TD of the second and third tests (Fig. 1E).

To study whether the W/WP experiences could influence the B/YP learning effect, the subjects were classified as the group with W/WP experience (n=22) and the group without previous W/WP experience (n=38). The differences of MD, PSD, and TD were respectively calculated between the first and the second tests ($MD_{1st\text{-}2nd}$, $PSD_{1st\text{-}2nd}$, $TD_{1st\text{-}2nd}$) and between the first and the third tests ($MD_{1st\text{-}3rd}$, $PSD_{1st\text{-}3rd}$, $TD_{1st\text{-}3rd}$). No statistically significant differences were noted in terms of $MD_{1st\text{-}2nd}$, $MD_{1st\text{-}3rd}$, $PSD_{1st\text{-}2nd}$, $PSD_{1st\text{-}3rd}$, $TD_{1st\text{-}2nd}$, and $TD_{1st\text{-}3rd}$ between the group with W/WP experience and the group without previous W/WP experience (Fig. 2, A–C).

To evaluate whether differences in B/YP learning effect existed among the normal subjects, patients with OHT, and patients with POAG, the subjects were divided into normal subject group (n=20), OHT group (n=26), and POAG group (n=14). The differences of MD, PSD, and TD were also respectively calculated between the first and the second tests ($MD_{1st\text{-}2nd}$, $PSD_{1st\text{-}2nd}$, $TD_{1st\text{-}2nd}$) and between the first and the third tests ($MD_{1st\text{-}3rd}$, $PSD_{1st\text{-}3rd}$, $TD_{1st\text{-}3rd}$). No statistically

significant differences were noted in terms of $MD_{1st\text{-}2nd}$, $MD_{1st\text{-}3rd}$, $PSD_{1st\text{-}2nd}$, $PSD_{1st\text{-}3rd}$, $TD_{1st\text{-}2nd}$, and $TD_{1st\text{-}3rd}$ among the normal subject group, OHT group, and POAG group (Fig. 3, A–C).

To study whether the refraction could influence the B/YP learning effect, the subjects were divided into the +5 D~0 D group (n=24), 0 D~–3 D group (n=22), and –3 D~–7 D group (n=14). The differences of MD, PSD, and TD were respectively calculated between the first and the second tests ($MD_{1st\text{-}2nd}$, $PSD_{1st\text{-}2nd}$, $TD_{1st\text{-}2nd}$) and between the first and the third tests ($MD_{1st\text{-}3rd}$, $PSD_{1st\text{-}3rd}$, $TD_{1st\text{-}3rd}$). No statistically significant differences were noted in terms of $MD_{1st\text{-}2nd}$, $MD_{1st\text{-}3rd}$, $PSD_{1st\text{-}2nd}$, $PSD_{1st\text{-}3rd}$, $TD_{1st\text{-}2nd}$, and $TD_{1st\text{-}3rd}$ among the three groups (Fig. 4, A–C). To evaluate whether the subject age could influence the B/YP learning effect, the subjects were divided into the 20~40 years group (n=16), 40~60 years group (n=30), and more than 60 years group (n=14). The differences of MD, PSD, and TD were also respectively calculated between the first and the second tests ($MD_{1st\text{-}2nd}$, $PSD_{1st\text{-}2nd}$, $TD_{1st\text{-}2nd}$) and between the first and the third tests ($MD_{1st\text{-}3rd}$, $PSD_{1st\text{-}3rd}$, $TD_{1st\text{-}3rd}$). No statistically significant differences were noted in terms of $MD_{1st\text{-}2nd}$, $MD_{1st\text{-}3rd}$, $PSD_{1st\text{-}2nd}$, $PSD_{1st\text{-}3rd}$, $TD_{1st\text{-}2nd}$, and $TD_{1st\text{-}3rd}$ among the three groups (Fig. 5, A–C).

DISCUSSION

In any new test, a learning effect could be present. The increase in sensitivity that has been documented as patients naive to perimetric testing become more experienced with the test is called the learning effect. In W/WP, the learning effect can influence the results of a visual field test. This perimetric effect has been observed in certain individuals, and it suggests that some patients need perimetric experience before producing test results that can be reliably reproduced and interpreted for clinical use. In these subjects, the initial visual field tests typically show the depressions that are sometimes substantial. As a consequence, perimetrically naive subjects in their initial field test may show abnormal results when judged by standard interpretation guidelines (28). The learning effect can be clinically relevant, causing an improvement in sensitivity (21, 29), but this effect was not confirmed by other authors (30, 31).

Many studies have suggested that B/YP is able to detect visual field loss in subjects with early glaucomatous damage (12-16, 32-34). However, before analyzing the effectiveness of B/YP in detecting early glaucomatous visual field loss, it is important to determine the learning effect in the healthy subjects, suspected glaucoma, and glaucoma patients. In our data, a learning effect was present, and it was statistically significant between the initial examination and any of the subsequent tests. Rossetti et al (23) and Wild et al (24) also found that a substantial B/YP learning effect existed in patients with OHT or open-angle glaucoma who were experienced in standard automated perimetry, but they did not study the B/YP learning effect in normal subjects and patients without previous W/WP experience. Our results showed that a significant learning effect was also present in normal subjects, and no significant difference was found in the B/YP learning effect among the normal subjects, OHT, and POAG. Even sub-

jects well trained with conventional automated perimetry showed a learning effect by B/YP. Therefore, one training session is recommended for the B/YP to avoid misinterpretation of results.

The influence of age on the W/WP learning effect has been reported by some studies (17, 18). Autzen and associates (17) found that the W/WP learning effect showed a positive correlation with age on mean sensitivity of the whole field; however, Kulze and associates (18) found that no significant difference was noted in learning effect based on age, sex, and race. Our result also showed that no significant difference was found in the B/YP learning effect among various age groups. Marra and Flammer (35) reported that patients with refractive errors, especially myopes, revealed a larger learning effect than did emmetropes. However, our data showed that no significant difference was found in the B/YP learning effect among various refraction groups.

In conclusion, our results suggested that a significant B/YP learning effect was present between the first and the second or third tests at full-threshold B/YP and the perimetric indices appeared improved in normal subjects and patients with OHT or POAG, and the previous W/WP experience and the subject age and refraction did not influence the B/YP learning effect. This above all should be taken into account when considering the clinical use of this test to avoid erroneous diagnostic conclusions.

None of the authors has proprietary interest in the development and marketing of any products mentioned in the article.

Reprint requests to:
Yisheng Zhong, MD
Department of Ophthalmology
Ruijin Hospital Affiliated Shanghai Jiaotong University
197 Ruijin No.2 Road
200025 Shanghai, China
yszhong68@yahoo.com.cn

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