Investigation

Visual disc parameters in healthy Zhuang and Han adults

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Foundation item: Guangxi Science Foundation Project, China (No. GKH0731011)

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Received: 2011-06-29 Accepted: 2012-02-09

Abstract

• AIM: To compare multiple visual disc parameters and the retinal morphology of healthy Zhuang adults with healthy Han adults.

• METHODS: Two equal cohorts of 120 healthy adults (480 eyes) of Zhuang and Han ancestry aged 20 to 60 years from unrelated families residing in Longlin County, Guangxi Zhuang Autonomous Region, China, for at least three generations were enrolled in this study. The visual disc parameters in Zhuang and Han populations were determined in four different age brackets (20-29, 30-39, 40-49, and 50-59) using Heidelberg retinal tomograph-II (HRT-II), and the relations between these parameters and race, gender, eye (left/right), and age were evaluated. The evaluated visual disc parameters included disc area $(DA mm^2)$, cup area $(CA mm^2)$, cup/disc area ratio(C/DAR), rim/disc area ratio (R/DAR), rim area (RA mm²), height variation contour (HVC mm), cup volume (CV mm³), rim volume (RV mm³), mean cup depth (MCD mm), maximal cup depth (MxCD mm), cup shape measure (CSM mm), mean retinal nerve fiber layer thickness (mRNFLT mm) and retinal nerve fiber layer area $(RNFLA mm^2).$

• RESULTS: There were significant difference in C/A, C/D, R/D, MCD, and MxCD between the ethnic two populations in the 30-39 year group (P < 0.05), and a significant difference in RA between the 50-59 year age groups(P < 0.05). No other statistically significant differences were observed for any other parameters. For both Zhuang and Han adults, mRNFLT and RNFLA were negatively correlated with age (correlation coefficients: -0.213 and -0.186 in the Zhuang population, -0.233 and -0.219 in the Han population). No statistical significance in these parameters was observed between males and females or between right and left eyes of the two ethnic populations. The C/DAR ratio difference between the left and right eyes ranged from 0.000 to 0.162 in the Zhuang population and from 0.048 to 0.112 in the Han population.

 \bullet CONCLUSION: There are few significant differences in

optic papilla contour parameters between healthy Zhuang and Han adults, except for the 30-39 age group, and there is no statistical difference in these visual disc parameters by gender or eye between the two populations.

• KEYWORDS: Zhuang people; Han people; visual disc parameters; retina tomography

DOI:10.3969/j.issn.1672-5123.2012.03.02

Li L, Yang K, Bai HQ. Visual disc parameters in healthy Zhuang and Han adults. *Guoji Yanke Zazhi(Int Eye Sci)* 2012;12(3): 384-387

INTRODUCTION

r he development of novel ophthalmic imaging techniques like Heidelberg retina tomography (HRT) now allows for the precise quantitative analysis of the ocular fundus, yielding new morphological parameters that may be useful in glaucoma research and disease diagnosis. The HRT device can provide an objective, reproducible, and real-time three-dimensional image of the fundus optic papilla and surrounding retina and perform a quantitative determination and contour analysis of the surface and depth of these tissues. The standard parameter values were obtained from the normal eyes of 122 Caucasian volunteers (mean age: 52 years), and was compared to the values from 77 Caucasian patients with early glaucoma (mean age: 62 years). Due to racial differences in eye parameters, the suitability of these values for research and clinical practice in the Asian populations is unclear. The Zhuang is the largest ethnic minority group in China. They are closely related to the Thai and Loatian population of Southeast Asia and have a unique position in the hereditary lineage of East Asians. Since more than 90% of Zhuang people live in Guangxi, China, we evaluated the parameters of the optic papilla contour map using HRT-II in healthy Zhuang adults native to Longlin County, Guangxi, and compared the findings to healthy majority Han adults from Guangxi. In addition to race, these parameters were analyzed against gender, eye side, and age group to establish baseline averages and variabilities for these Asian populations.

MATERIALS AND METHODS

Materials To insure that the subjects in this study were of definitive Han or Zhuang ancestry, we screened candidates according to family history, language, and place of residence. Zhuang participants must have come from settlements where the Zhuang accounted for more than 85% of the population and could document Zhuang origin, spoke the Zhuang language and could prove absence of intermarriage for at least three generations. Only individuals of the third generation

Int Eye Sci, Vol. 12, No. 3, Mar. 2012 www.ies. net. cn Tel:029-82245172 82210956 Email: IJO. 2000@163. com

 Table 1 Overall optic papilla contour parameters between Zhuang and Han populations

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Parameter	All age		20-29 yers		30-39 yers		40-49 yers		50-59 yers	
	Zhuang	Han								
$DA(mm^2)$	2.26 ± 0.47	2.22 ± 0.43	2.28 ± 0.52	2.20 ± 0.49	2.17 ± 0.48	2.28 ± 0.42	2.29 ± 0.45	2.22 ± 0.39	2.29 ± 0.41	2.16 ± 0.40
$CA(mm^2)$	0.51 ± 0.35	0.48 ± 0.30	0.49 ± 0.34	0.50 ± 0.36	0.37 ± 0.35	0.51 ± 0.30	0.60 ± 0.32	0.42 ± 0.23	0.54 ± 0.38	0.51 ± 0.28
$RA(mm^2)$	1.75 ± 0.35	1.73 ± 0.32	1.79 ± 0.39	1.71 ± 0.32	1.79 ± 0.40	1.77 ± 0.33	1.68 ± 0.31	1.79 ± 0.32	1.75 ± 0.27	1.66 ± 0.32
C/DAR	0.21 ± 0.12	0.21 ± 0.11	0.20 ± 0.12	0.21 ± 0.13	0.16 ± 0.12	0.22 ± 0.11	0.25 ± 0.11	18 ± 0.11	0.22 ± 0.12	0.22 ± 0.11
R/DAR	0.80 ± 0.12	0.79 ± 0.11	0.80 ± 0.12	0.79 ± 0.13	0.84 ± 0.12	0.78 ± 0.11	0.75 ± 0.11	0.82 ± 0.11	0.78 ± 0.12	0.79 ± 0.11
$CV(mm^3)$	0.12	0.11	0.10	0.13	0.11	0.11	0.14	0.14	0.12	0.11
$RV(mm^3)$	0.53 ± 0.14	0.52 ± 0.15	0.55 ± 0.21	0.54 ± 0.16	0.60 ± 0.19	0.55 ± 0.17	0.49 ± 0.13	0.54 ± 0.13	0.50 ± 0.15	0.46 ± 0.13
MCD(mm)	0.21 ± 0.10	0.21 ± 0.08	0.21 ± 0.12	0.21 ± 0.22	0.18 ± 0.14	0.22 ± 0.14	0.24 ± 0.04	0.19 ± 0.04	0.20 ± 0.12	0.21 ± 0.12
MxCD(mm)	0.60 ± 0.22	0.60 ± 0.19	0.58 ± 0.21	0.63 ± 0.22	0.56 ± 0.21	0.64 ± 0.18	0.67 ± 0.23	0.57 ± 0.18	0.58 ± 0.22	0.58 ± 0.19
HVC(mm)	0.45 ± 0.10	0.45 ± 0.16	0.44 ± 0.10	0.46 ± 0.10	0.47 ± 0.10	0.50 ± 0.29	0.46 ± 0.12	0.44 ± 0.12	0.42 ± 0.10	0.41 ± 0.10
CSM(mm)	-0.20 ± 0.07	-0.22 ± 0.06	-0.20 ± 0.01	-0.22 ± 0.01	-0.23 ± 0.02	-0.23 ± 0.02	-0.19 ± 0.01	-0.24 ± 0.01	-0.20 ± 0.02	-0.19 ± 0.02
mRNFLT(mm)	0.30 ± 0.07	0.31 ± 0.08	0.31 ± 0.01	0.34 ± 0.12	0.32 ± 0.02	0.31 ± 0.02	0.30 ± 0.21	0.30 ± 0.21	0.27 ± 0.12	0.31 ± 0.12
$RNFLA(mm^2)$	1.57 ± 0.43	1.58 ± 0.38	1.65 ± 0.42	1.66 ± 0.39	1.64 ± 0.42	1.66 ± 0.96	1.6 ± 0.48	1.56 ± 0.37	1.45 ± 0.38	1.58 ± 0.38

were recruited as subjects. The Han subjects were enrolled from Han settlements in Guangxi following three criteria: three generations of Han origin, Mandarin as the first language, and maintaining Han family names. Our research team went to Longlin autonomous county where five races, including Miao, Yi, Gelao, Zhuang, and Han have settled. Within the county, most of the Zhuang resided in Bianya village and most Han in Longhuo village. A total of 240 healthy Zhuang and Han subjects (120 eves per group for a total of 480 eves) were enrolled. All subjects provided written informed consent in conformance to the Helsinki Declaration. In the Zhuang population, there were 56 males (112 eyes) and 64 females (128 eyes). In Han population, there were 51 males (102 eves) and 69 females (138 eves). All the subjects were between 20 and 59 years at the initiation of the study and were divided into four age brackets: 20-29, 30-39, 40-49, and 50-59 years of age. Each age bracket contained 30 subjects (60 eyes) per ethnic group. The inclusion criteria for a "healthy" adult included normal visual function, bilateral corrected visual acuity ≥ 1.0 , diopter within $\pm 5.0D$ (corrected), intraocular pressure ≤ 21 mmHg, fundus C/D < 0.5, absence of craniocerebral or optic nerve related disease and systemic disorders, no family history of glaucoma or retinal vascular disease, and the availability of clear images by HRT with double peaks. The exclusion criteria included anterior optic neuropathy, ocular media opacity (by slit-lamp examination), and blurred vision or abnormal visual field findings.

Methods The examination was performed using a type 2.01 HRT manufactured by Heidelberg Corporation (Germany), with designated examining scope at $15^{\circ} \times 15^{\circ}$, scanning depth range of 0.5-4.0mm and regulated diopter range of $\pm 11.0D$. Three serial images were obtained from each eye without dilating the pupils and data were recorded to compact disc. A mean contour map could be obtained from the three images and the reference plane designated in this study was the standard reference plane set in the device. The optic papilla contour was also generated by the same operator (Bai HQ) to obtain the values of the optic papilla parameters in this mean

contour map. The visual disc parameters evaluated were disc area (DA mm^2), cup area (CA mm^2), cup/disc area ratio (C/DAR), rim/disc area ratio (R/DAR), rim area (RA mm^2), height variation contour (HVC mm), cup volume (CV mm^3), rim volume(RV mm^3), mean cup depth(MCD mm), maximal cup depth(MxCD mm), cup shape measure(CSM mm), mean retinal nerve fiber layer thickness (mRNFLT mm), and retinal nerve fiber layer area (RNFLA mm^2).

Statistical Analysis The K-S normal distribution test and analysis of means were performed on the 13 optic papilla parameters. The comparisons by gender and eye side were performed using two-sample *t*-tests. The comparison of disc area between age groups was performed using ANOVA. The correlation between age and each of the 13 parameters was evaluated using linear regression analysis. The correlation between each parameter and race, age, gender, and eye was evaluated using multivariate analysis. Differences in variability of the parameters between Zhuang and Han populations were assessed using two-sample *t*-tests.

RESULTS

Average values of the visual disc parameters for the Zhuang and Han subjects (n = 120 for each ethnic group) are shown in Table 1. There was significant variation in all visual disc parameters in both Zhuang and Han populations, with a coefficient of variation range of 19. 7-69. 5% for Zhuang subjects and 13.7-61.8% for Han subjects. The parameters with greatest variability were CA, C/DAR, MCD, and MxCD, while those with the least variability were related to the nerve fiber layer, including RA, RV, mRNFLT, and RNFLA. There were no significant differences in the average value of any of the parameters between the Zhuang and Han males or females (P = 0.158 - 0.675) as determined by twosample *t*-tests. There were no significant differences in these parameters as measured in the left and right eyes of healthy Zhuang and Han subjects (P = 0.063-0.895). The 95% confidence interval of C/DAR differences ranged from 0.000-0.162 in the Zhuang population and from 0.048-0.112 in the Han population. While no significant differences in visual disk parameters where found in the overall means, differences

were observed between populations when stratified by age. Significant differences were observed in CA, C/D, R/D, MCD, and MxCD in the 30-39 age bracket and for RA in the 50-59 year age bracket. Correlational analysis revealed no significant correlation between age and these parameters, except for mRNFLT and RNFLA, which were negatively correlated with age (P = 0.001 and 0.044 in Zhuang subjects; P = 0.000 and 0.001 in Han subjects). The equations obtained by linear regression of age versus mRNFLT (Y1) or RNFLA(Y2) are presented (Table 1, 2).

DISCUSSION

There are few documented accounts of the important events in Zhuang history due to the absence of their own written language until the modern era when the Zhuang people began to receive training in Chinese. Thus, little is known of the genetic history and epidemiology of this population. Glaucoma is a common ophthalmological disease, causing abnormalities in the optic papilla and retinal nerve fiber layer prior to any changes in visual acuity. Therefore, preclinical parameters are important for early diagnosis. Studying the distribution of the various features of the normal visual disc in healthy adults in different races will not only help elucidate genetic differences in visual function between races, but also provide race-specific baseline values and deviation thresholds for the early diagnosis of glaucoma. In order to obtain the normal visual disc parameter values of Zhuang adults, our research team conducted a large-scale field investigation in a Zhuang settlement in Guangxi that validated pervious reports and data from authorities. We established a strict subject screening procedure for clear identification of Zhuang subjects and used healthy Han residents from the same region as the control population. While this selection procedure greatly reduced the number of eligible candidates, it resulted in greatly improved reliability of the interracial comparison. In the present study, the healthy subjects were defined as having normal visual function by bilateral corrected visual acuity ≥ 1.0 , diopter within $\pm 5.0D$ (corrected with eye glasses), intraocular pressure ≤ 21 mmHg, fundus C/D < 0.5, no evidence of craniocerebral or optic nerve related disease or other systemic disorders, no family history of glaucoma or retinal vascular disease, and the availability of clear images by ONH with double peaks. This study required high compliance, so only healthy subjects from 20 to 60 years of age were considered.

Distinguishing healthy subjects from glaucoma patients using visual disc parameters like disc size, cup size, and depth, or retinal nerve fiber thickness, is difficult due to the great variation in normal adults and overlap with values from patients with early glaucoma ^[1]. Moreover, the ONH variation should be taken into consideration when evaluating glaucoma and other optic nerve diseases between the races ^[2]. The standard parameter values of the HRT-II used in the present study are based on the normal eyes of a Caucasian population. As revealed in the present study, the values of visual cup parameters, such as CA, C/DAR, and CV, were similar in healthy Zhuang and Han subjects. The mean visual disc area

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Table 2Correlations between optic papilla contour parametersand age in Zhuang and Han populations

and age in Zhuang and man populations								
Parameter	r	Р	Linear regression					
mRNFLT in Zhuang	-0.213	0.001	Y = 0.356 - 0.001X					
mRNFLT in Han	-0.233	0.000	Y = 0.373 - 0.001X					
RNFLA in Zhuang	-0.186	0.004	Y = 1.863 - 0.007X					
RNFLA in Han	-0.219	0.001	Y = 1.863 - 0.006X					

value in the Zhuang population was 2.26 ± 0.47 mm², slightly greater than that reported previously by Liu $et al^{[3]}$ from 116 healthy Chinese adults. This discrepancy may be the result of the diopter and/or educational level of the subjects, insufficient sample size, or uncontrolled genetic variability. This value was also similar to that reported by Nakamura $et al^{[4]}$ from Japanese volunteers $(2.15 \pm 0.50 \text{ mm}^2)$, but lower than that reported by Agarwal et al^[5] from Indians (2.34 ± 0. 47 mm^2). Krueger *et al*^[6] compared 225 Caucasian Swiss and 1027 African Congolese; the visual disc area value in Caucasians was greater than in Africans (DA ratio of 2.56:1.81), and the visual disc area of this African population was lower than observed in our Asian study, indicating significant racial differences in DA. There was no significant difference in any of the visual disc parameters examined between male and female of the two ethnic groups or between left and right eyes, consistent with results reported by Xia et al^[7] and Agarwal et $al^{[5]}$. This result may be related to the consistency of the anatomical visual disc structure between male and female and between the right and left eyes in individuals.

The incidence of glaucoma in the general Chinese population is 0.68%, but increases with age to 47% at 65 years of age and older. Since age is a glaucoma-related risk factor, we stratified the subject population by age group, taking a 10year interval as an age bracket. We found no statistically significant differences between aged-matched Zhuang and Han subjects with the exception of CA, C/D, R/D, MCD, and MxCD in the 30-39 year age bracket and RA in the 50-59 year old groups. Regression analysis revealed that age was negatively correlated with mRNFLT and RNFLA (Zhuang population: -0. 213 and -0. 185; Han population: -0. 233 and -0.219, respectively). Regression analysis predicted that the thickness of the RNFL would decrease by 0.001mm per year, similar to conclusion of Nakamura $et al^{[8]}$. This RNFL thinning is caused by age-dependent loss of retinal nerve fibers and changes in the composition and proportion of certain extracellular matrix components in the visual disc (mainly collagens type II, III and IV, elastin, and membrane proteins). Even in healthy subjects, retinal ganglion cells can undergo apoptosis with age, resulting in a reduction in retinal nerve fiber axons and decreased RNFL thickness. Xiao $et al^{[9]}$ reported that the thickness of the RNFL was reduced by 0.002mm/year, so our study yielded similar estimates.

Although there were some race-specific characteristics in

Zhuang population, this study shows that there are no marked differences in the optic papilla structure between Zhuang and Han populations in Guangxi, China. Age has a little influence on most visual disc contour parameters. In present study, a normal range for these parameters in the Zhuang population is provided as a baseline for future basic research and clinical studies. In the future, our research team will focus on the glaucoma data of Zhuang adults in Guangxi, which may provide a meaningful tool for evaluating the causality between visual disc parameters and corresponding diseases.

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广西地区壮族和汉族正常成人视盘参数的观察

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基金项目:广西科学基金项目(No. 桂科回 0731011)

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摘要

目的:研究广西地区壮族和汉族正常成年人(20~60岁) 视盘参数正常值及其形态特征,比较其在不同民族间的差异。 方法:将3代居住广西隆林县无血缘关系的240例正常人 (壮、汉族各120例480眼)纳入研究。运用海德堡视网膜 断层扫描仪(Heidelberg retina tomograph-II,HRT-II)分别 检测不同年龄段壮族与汉族人群视盘参数,并探讨民族、 性别、眼别、年龄与视盘参数的关系。视盘参数包括视盘 面积(DA mm²)、视杯面积(CA mm²)、视杯/视盘面积比值 (C/DAR)、盘沿/视盘面积(R/DAR)、盘沿面积(RA mm²)、 视乳头轮廓线高度变化值(HVC mm)、视杯容积(CV mm³)、 盘沿容积(RV mm³)、平均视杯深度(MCD mm)、最大视杯 深度(MxCD mm)、视杯形态测量(CSM mm)、平均视网膜 神经纤维层厚度 mRNFLT mm)、视网膜神经纤维层截面 面积(RNFLA mm²)。

结果:按年龄分成4组,两民族间比较:CA、C/D,R/D, MCD,MxCD参数在30~39岁组有显著差异(P<0.05), RA参数在50~59岁组有显著差异(P<0.05),其余参数 在各年龄段无显著差异。正常壮、汉族人 mRNFLT 和 RNFLA 值与年龄均呈负相关,壮族相关系数分别为-0.213 和-0.186,汉族相关系数分别为-0.233和-0.219,性别间 各参数差异无显著意义,眼别间差异无显著意义。壮族 C/DAR 比值双眼差值范围为 0.000~0.162。汉族 C/D AR 比值双眼差值范围为为 0.048~0.112。

结论:两民族视乳头地形图参数无显著差异。年龄对视乳 头地形图某些参数有一定影响,而性别间、眼别视盘各参 数间差异无显著意义。

关键词:壮族;汉族;视盘参数;视网膜断层扫描