

doi: 10.3978/j.issn.1000-4432.2017.12.04

View this article at: <http://dx.doi.org/10.3978/j.issn.1000-4432.2017.12.04>

· 论著 ·

健康中老年人中心视觉敏感度与光相干断层扫描血管成像的双眼对称性

刘瑞¹, 李轻宸²

(1. 同济大学附属第十人民医院眼科, 上海 200072; 2. 复旦大学附属眼耳鼻喉科医院眼科, 上海 200031)

[摘要] 目的: 观察健康中老年人群中中心凹视觉敏感度阈值(foveal threshold, FT)及光相干断层扫描血管成像(optical coherence tomography angiography, OCTA)的双眼对称性。方法: 横断面观察性研究。纳入33例66眼, 测量并比较眼灌注压(ocular perfusion pressure, OPP), FT, 黄斑区3 mm × 3 mm范围内中心凹无血管区面积(non-flow area, NFA), 浅层视网膜血管密度(superior vessel density, SVD)和深层视网膜血管密度(deep vessel density, DVD)的双眼对称性; 分析各指标双眼差值、均值及其比值与年龄、性别的相关性。结果: 配对样本 t 检验结果显示除FT($t=-2.118$, $P=0.042$)外, 左右眼OPP, NFA, SVD和DVD差异均无统计学意义($P>0.05$); Pearson相关性分析和同类相关系数(intra-class correlation coefficient, ICC)检验结果显示5项指标左右眼测量值相关强度由强到弱为OPP>FT>NFA>DVD>SVD; Bland-Altman分析结果提示5项指标双眼间一致性良好。5项指标的双眼对称性不随性别、年龄改变。结论: 健康中老年人群中FT、黄斑区NFA, SVD及DVD的测量值具有双眼对称性。

[关键词] 光相干断层扫描血管成像; 中心凹视觉敏感度阈值; 双眼对称性; Bland-Altman检验

Interocular symmetry of foveal threshold and optical coherence tomography angiography in healthy middle-aged and elderly subjects

LIU Rui¹, LI Qingchen²

(1. Department of Ophthalmology, Tenth People's Hospital of Tongji University, Shanghai 200072;

2. Department of Ophthalmology, Eye and ENT Hospital of Fudan University, Shanghai 200031, China)

Abstract **Objective:** To observe the interocular symmetry of foveal threshold (FT) and optical coherence tomography angiography (OCTA) parameters in healthy middle-aged and elderly subjects. **Methods:** Cross-sectional observational study. Sixty-six eyes from thirty-three subjects were enrolled to compare binocular ocular perfusion

收稿日期 (Date of reception): 2017-11-26

通信作者 (Corresponding author): 李轻宸, Email: qcli16@fudan.edu.cn

pressure (OPP), FT, non-flow area (NFA), superior vessel density (SVD) and deep vessel density (DVD) in a 3 mm × 3 mm OCTA scan of macula. The interocular symmetry of all the parameters was analyzed; the correlations of the differences (Δ), mean value (m) and the ratio of all the parameters with age and gender were analyzed. **Results:** There was no significant interocular difference revealed by paired-samples t -tests in all the parameters ($P>0.05$) except FT ($t=-2.118, P=0.042$), while the rank of Pearson's correlation index and intra-class correlation coefficient (ICC) from strong to weak was OPP > FT > NFA > DVD > SVD. The interocular symmetry of all the parameters was proved to be good with Bland-Altman plots, and it changed little with the variations of age and gender. **Conclusion:** Interocular symmetries of FT and OCTA parameters are observed in healthy middle-aged and elderly subjects.

Keywords optical coherence tomography angiography; foveal threshold; interocular symmetry; Bland-Altman

光相干断层扫描因非接触、分辨率高、客观精确、重复性好等优势,广泛应用于多种眼病及眼部结构性改变的检查;有报道^[1-2]借助该技术发现正常个体眼球在前后节段解剖结构上具有双眼对称性。光相干断层扫描血管成像(optical coherence tomography angiography, OCTA)作为在此基础上发展的新型血管影像学工具,其能够分层观察视网膜脉络膜血管形态及血流改变情况,区分正常与异常的血管结构,并对血流信号进行探测和量化分析。目前少有关正常个体双眼间功能学参数对称性的研究,本文选择中心凹视觉敏感度阈值(foveal threshold, FT)作为视功能评估指标,结合OCTA参数,分析健康中老年人群的双眼对称性,以加深对眼部生理学的认知。

1 对象与方法

1 对象

经所在单位医学伦理委员会批准,所有受试者知情并签署同意书。2017年1至6月于同济大学附属第十人民医院眼科门诊选取受试者接受血压测量(systolic blood pressure/diastolic blood pressure, SBP/DBP)、双眼非接触眼压(intraocular pressure, IOP)、裂隙灯检查、直接眼底镜检查及综合验光仪验光。

纳入标准:年龄45~74岁;最佳矫正视力(best corrected visual acuity, BCVA)≥0.4;等效球镜屈光度为-6.0~+1.0 D; IOP为10~21 mmHg (1 mmHg=0.133 kPa);裂隙灯显微镜检查确认眼前段结构正常、屈光间质透明;视盘C/D≤0.6且双眼相差不超过0.2;双眼眼位正常,中心固视良好。

排除标准:1)除屈光不正以外存在其他影响

视功能的眼部疾病、外伤及内眼手术史;2)接受过角膜屈光手术、人工晶状体植入术,或于检查当日配戴隐形眼镜等影响屈光度判断;3)明确的青光眼及视网膜疾病家族史;4)有严重影响眼部健康的系统疾病,如高血压、糖尿病、甲状腺功能障碍、风湿免疫性疾病等;5)因不能理解配合仪器测试或屈光间质混浊造成图片信号强度评分(signal strength index, SSI)低于38者^[3]。

1.2 方法

采用标准自动视野计Humphrey Field Analyzer II,在10-2瑞典相关阈值算法(Swedish Interactive Thresholding Algorithm, SITA)模式下获取FT,测量3次记录其平均值(dB)。该参数预先经倒数化运算,显示值越高,表示对光敏感度越高,黄斑区反应越灵敏;反之,对光敏感度越低,黄斑区越迟钝。

采用RTVue100光相干断层扫描血管成像系统(美国OPTOVUE公司),选取AngioVue Retina模式,嘱受试者注视蓝色视标保持3 s,依次完成横向和纵向扫描,每个区域扫描2次,保留清晰度最高的图像。内置系统据此测算黄斑区3 mm × 3 mm范围内中心凹无血管区面积(non-flow area, NFA)、浅层视网膜血管密度(superior vessel density, SVD)和深层视网膜血管密度(deep vessel density, DVD)3项指标。

1.3 统计学处理

应用SPSS 24.0统计学软件进行分析。计算平均动脉压(mean arterial pressure, MAP)=(SBP+2×DBP)/3,眼灌注压(ocular perfusion pressure, OPP)为2×MAP/3-IOP^[4];

计算OPP, FT, NFA, SVD和DVD共5项指标的双眼间差值(Δ , 右眼-左眼)、平均值(mean, 右眼测量值/2+左眼测量值/2)及差值百分比($\Delta/\text{mean}\times 100\%$)。配对样本 t 检验比较左右眼各指标差异, 独立样本 t 检验比较男女性别各指标差异; 采用Pearson相关性系数、同类相关系数(intra-class correlation coefficient, ICC)和Bland-Altman图(MedCalc 17.6)评价各指标左右眼一致性。以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 左右眼对称性分析

研究纳入男性9例(27.27%), 年龄(52.89 ± 6.29)岁; 女性24例(72.73%), 年龄(50.46 ± 6.85)岁, 男女年龄差异无统计学意义($t=-0.926, P=0.361$)。

除右眼FT略小于左眼外, 双眼间OPP, NFA, SVD和DVD的差异无统计学意义($P<0.05$, 表1)。

相关性检验结果显示: 5项指标双眼间均显著相关, 其关联强度由强到弱依次为OPP>FT>NFA>DVD>SVD(表2)。

Bland-Altman图中, 5项指标双眼间差值均有超过95%的点处于一致性界限(Limits of Agreement, LoA)95%可信区间(LoA CI)内, 提示OPP, FT, NFA, SVD和DVD双眼间一致性良好。其中, OPP和DVD所有样本点均在LoA CI范围内(100%), FT, NFA及SVD均有32个样本点位于LoA CI范围内(96.97%, 图1)。

2.2 各指标双眼间差值、平均值和差值百分比与年龄、性别的分析

受试者左右眼间 Δ OPP为 0.18 ± 2.59 (95%CI $-0.73\sim 1.11$) mmHg; Δ FT为 -0.58 ± 1.56 (95%CI $-1.09\sim -0.06$) dB; Δ NFA为 0.02 ± 0.11 (95%CI $-0.01\sim 0.06$); Δ SVD为 $0.71\%\pm 3.97\%$ (95%CI $-0.71\%\sim 1.94\%$); Δ DVD为 $0.17\%\pm 2.83\%$ (95%CI $-0.93\%\sim 1.10\%$)。

Pearson相关性检验结果显示: 随年龄增长, 左右眼 Δ NFA和mNFA增大, mFT, mSVD, mDVD减小, 其余参数不变。独立样本 t 检验显示: 男女性别间5项指标差值、平均值和差值百分比差异均无统计学意义(表3~5)。

表1 各指标左右眼测量值比较

Table 1 Comparison of measurements of right and left eye

类别	OPP/mmHg	FT/dB	NFA/mm ²	SVD/%	DVD/%
右眼值	50.37 \pm 5.12	33.39 \pm 2.75	0.36 \pm 0.17	52.98 \pm 3.88	57.15 \pm 3.38
左眼值	50.19 \pm 6.22	33.97 \pm 2.30	0.34 \pm 0.14	52.27 \pm 3.25	56.99 \pm 2.51
t	0.397	-2.118	1.068	1.032	0.335
P	0.694	0.042	0.293	0.31	0.74

表2 各指标的双眼相关性系数

Table 2 Correlation between measurements of right and left eye

类别	OPP		FT		NFA		SVD		DVD	
	r	P	r	P	r	P	r	P	r	P
ICC	0.946	<0.001	0.895	<0.001	0.848	<0.001	0.554	0.013	0.708	<0.001
R值	0.914	<0.001	0.823	<0.001	0.759	<0.001	0.389	0.025	0.572	0.01

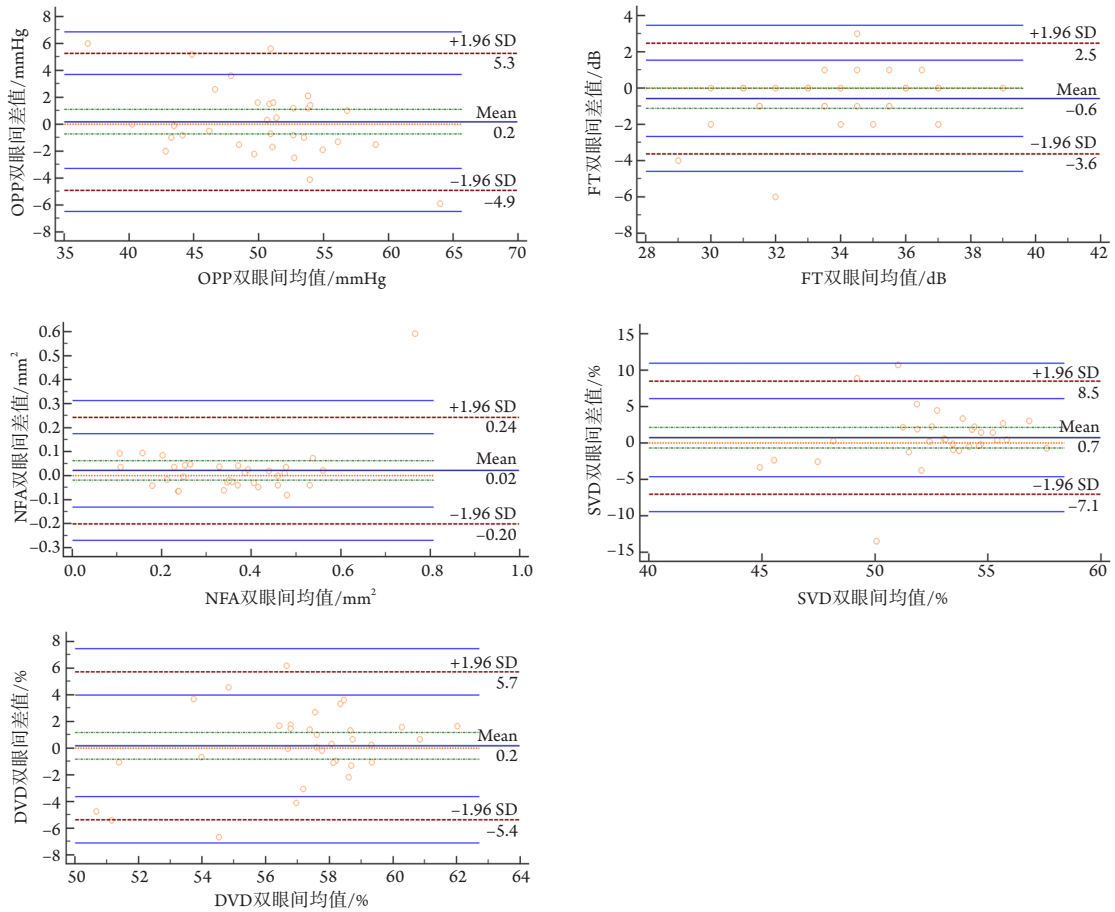


图1 各指标左右眼测量值的Bland-Altman散点图
Figure 1 Bland-Altman plots of parameters of right and left eye

表3 各指标的双眼间差值与年龄、性别的相关性

Table 3 Correlation between interocular differences and age, sex

类别	△OPP	△FT	△NFA	△SVD	△DVD
年龄					
<i>r</i>	-0.018	-0.145	0.528	-0.207	-0.311
<i>P</i>	0.922	0.419	0.002	0.248	0.078
性别					
<i>t</i>	-1.215	-0.792	1.287	0.188	-0.088
<i>P</i>	0.233	0.435	0.207	0.852	0.931

表4 各指标的双眼间均值与年龄、性别的分析

Table 4 Correlation between interocular mean values and age, sex

类别	mOPP	mFT	mNFA	mSVD	mDVD
年龄					
<i>r</i>	-0.162	-0.635	0.455	-0.526	-0.530
<i>P</i>	0.369	<0.01	0.008	0.002	0.002
性别					
<i>t</i>	0.966	1.164	-0.077	0.006	0.834
<i>P</i>	0.356	0.253	0.939	0.995	0.411

表5 各指标的双眼间差值百分比与年龄、性别的分析

Table 5 Correlation between percentile interocular differences and age, sex

类别	%OPP	%FT	%NFA	%SVD	%DVD
年龄					
<i>r</i>	0.008	-0.193	0.120	-0.217	-0.322
<i>P</i>	0.965	0.282	0.506	0.225	0.068
性别					
<i>t</i>	-1.389	-0.815	1.804	0.295	-0.061
<i>P</i>	0.175	0.421	0.081	0.77	0.952

3 讨论

根据联合国WHO年龄划分标准, 45~59岁为中年人, 60~74岁为年轻老年人。随着人均寿命的提高, 人口老龄化已成为全球性的社会问题^[5]。高龄被认为是诸多眼部疾病的危险因素, 包括白内障^[6]、青光眼^[7]、黄斑变性^[8]、缺血性视神经病变^[9]和干眼^[10]等; 与此对应的, 病理学研究^[11]发现人类眼球的各部位组织均存在年龄相关的结构改变。双眼对称性被视为判断双眼是否存在不对称性病理改变的重要指标。已有多篇文献从不同方面证实健康人类双眼间对称性良好: 如瞳孔对光反应^[12-13]、眼球突出度^[14-15], 又如视网膜神经纤维层厚度^[16-17]和神经节细胞复合体厚度^[18-19]等。但上述报道多集中于双眼间解剖结构的对称性, 本研究在现有基础上, 针对中老年人群, 引入功能学指标FT和可量化血流灌注的OCTA, 拓展了对眼部生理学的认知。结果显示: 健康中老年人在视觉敏感度和视网膜血供方面同样具有较好的双眼对称性。

Flaxel等^[20]报道FT与BCVA间存在高度相关性,

可作为量化评估视功能的可靠指标。近年来, 相继有研究^[21-23]发现黄斑增厚性疾病、视网膜色素变性和青光眼患者的FT同样与BCVA保持较好的一致性; 相比之下, BCVA是基于红绿测试平衡点的主观结果, 较大程度依赖验光师经验和受试者配合程度, 因此本研究选取FT代替BCVA作为反映视功能的指标。但同时, 光敏感度阈值测量仍属于心理物理学方法, 受被测试者情绪、心理状态、认知力及配合程度等影响。另一方面, 本研究所用设备采用分频谱振幅去相干血管成像(Split Spectrum Amplitude Decorrelation Angiography, SSADA)算法, 其原理为将原始全频谱图像分裂为数个不同频谱图像并减少其噪声, 提高信噪比后再行合并, 从而得到横断面血管形态的成像^[24]。黄斑区NFA, SVD及DVD均为常见的视网膜血液灌注流量量化指标^[25]。基于SSADA算法量化的健康人群黄斑区NFA^[26-28]及SVD、DVD^[29-31]均有较高可重复性和再现性。这在一定程度上可解释本研究结果中主观测量得到的FT值在左右眼间差异有统计学意义, 而客观测量所得的OCTA各参考值在配对*t*检验

结果中具有更小的双眼间差异。矛盾的是, NFA, SVD, DVD三项指标左右眼测量值的Pearson相关系数和ICC均低于FT, 提示前三者左右眼测量值的一致性较弱。尽管配对样本 t 检验和简单相关性分析都是评估两组数据一致性的常用统计学方法, 二者在本研究中对FT与OCTA参数双眼一致性的检验结果却不一致。配对样本 t 检验仅比较两组数据差值所代表的总体其均数与0之间差异是否有统计学意义, 对随机误差的检出不敏感; 而简单的相关性分析对系统误差的识别能力较差, 人为地按比例放大或缩小两组待检数据中的其中一组, 相关系数可不变; 因此有学者^[32]提出该两种方法均不应单独使用。Bland-Altman分析作为新兴的图形化分析方法, 可从集中趋势、离散趋势及同步变化程度3个方面对两组定量资料进行全面的一致性评价^[33], 现已成为首选统计学方法。本研究中Bland-Altman检验结果说明OPP, FT, NFA, SVD和DVD等5项指标的双眼间一致性良好, 即正常中老年人以上指标双眼对称。其中, OPP双眼间差值实质为眼压差值, 已知国人眼压正常值双眼对称、且差异不超过5 mmHg^[34-35], 而 Δ OPP的95%分布范围, 即LoA上下界分别为-4.9和5.3 mmHg, 也与既有认识相符。

除 Δ NFA外, 其余各指标的双眼间差值均不随年龄和性别改变, 这进一步验证上述对称性是本文受检人群的固有属性; 而尽管NFA的差值绝对值与年龄呈正相关, 其均值也以相近的变化率随年龄改变, 而NFA双眼差值与均值的比例未发生变化可理解为 Δ NFA绝对值的增加是由于基础值按比例放大而非双眼对称性发生改变。此外, 在OPP均值未出现显著降低的情况下, mNFA, mSVD和mDVD这3项指标随年龄的改变提示眼部血流灌注程度下降, 二者之间的关联值得进一步探讨。

总而言之, 本研究发现健康中老年人群的FT和OCTA指标具有较好双眼对称性; 但因样本量小、种族单一、参考指标偏少、欠缺对照等原因, 视功能和血流灌注情况双眼对称性的价值还有待后续研究拓展。

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本文引用: 刘瑞, 李轻宸. 健康中老年人中心视觉敏感度与光相干断层扫描血管成像的双眼对称性[J]. 眼科学报, 2017, 32(4): 199-205. doi: 10.3978/j.issn.1000-4432.2017.12.04

Cite this article as: LIU Rui, LI Qingchen. Interocular symmetry of foveal threshold and optical coherence tomography angiography in healthy middle-aged and elderly subjects[J]. Yan Ke Xue Bao, 2017, 32(4): 199-205. doi: 10.3978/j.issn.1000-4432.2017.12.04