Abnormal Cambridge low-contrast grating sensitivity results associated with diabetic retinopathy as a potential screening tool

M. Abrishami,[1] J. Heravian,[2] A. Derakhshan,[1] M. Mousavi,[1] T. Banaee,[1] R.Daneshvar[1] and H.O. Moghaddam[2]

قيمة النتائج غير الطبيعية لاختبار حساسية الحزيز المنخفض التباين، المصاحبة لاعتلال الشبكية السكّري، كأداة محتملة لتحرّي هذا الاعتلال

مجيد ابريشمي، جواد هرويان، أكبر درخشان، ميرنقي موسوي، توكا بنايي، رامين دانشور كاخكي، هادي استادي مقدم

الخلاصة: اقترحت الحساسية التباينية لتكون أداة محتملة لتحرِّي اعتلال الشبكية السكَّري. وقد أُجريت دراسة مستعرضة في مركز لرعاية العيون في مستشفى إحالة تخصُّصي جامعي. وتم استدعاء 80 من مرضى السكَّري وبلغ عدد العيون التي اختُبِرَتْ 154 عيناً. وتم فحص الحساسية التباينية باستخدام حزيز grating كمبريدج المنخفض التباين. ولوحظت حساسية تباينية شاذة في 27.1٪ من العيون المصابة باعتلال الشبكية السكَّري، بالمقارنة مع 9.0٪ في العيون غير المصابة، وهو فارق يُعْتَدُّ به إحصائياً. واستنتجت الدراسة أن حزيز كمبريدج المنخفض التباين هو أحد الأدوات المحتملة التي يمكن لغير أطباء العيون استخدامها في التحرِّي المبكِّر لاعتلال الشبكية السكَّري.

ABSTRACT Contrast sensitivity is proposed as a potential screening tool for the early detection of diabetic retinopathy. A cross-sectional study was performed in a tertiary referral university eye centre. A total of 80 diabetes patients were recruited and tests were performed on 154 eyes. Contrast sensitivity was checked using Cambridge low-contrast grating. Abnormal contrast sensitivity was observed in 27.1% of eyes with diabetic retinopathy, compared with 9.0% in unaffected eyes, a statistically significant difference. Cambridge low-contrast grating is a potential screening tool for early detection of diabetic retinopathy by non-ophthalmologists.

Les anomalies au test optométrique CLCG (*Cambridge low-contrast grating sensitivity*) comme outil potentiel de dépistage de la rétinopathie diabétique

RÉSUMÉ On suggère l'utilisation de la sensibilité au contraste comme outil potentiel de dépistage dans le cadre de la détection précoce de la rétinopathie diabétique. Un centre ophtalmologique universitaire de référence en soins tertiaires s'est livré à une étude transversale portant au total sur 80 patients diabétiques, ce qui représente l'exploration de 154 yeux. La sensibilité au contraste a été évaluée *via* un test CLCG (pour *Cambridge low-contrast grating*.) Une sensibilité anormale au contraste a été observée dans 27,1 % des yeux atteints de rétinopathie diabétique, contre 9,0 % des yeux indemnes de cette pathologie, écart qui représente une différence statistiquement significative. Le test CLCG constitue un outil potentiel de dépistage précoce de la rétinopathie diabétique utilisable par tout professionnel de santé non spécialisé en ophtalmologie.

[1]Department of Ophthalmology, Khatam Al-Anbia University Eye Hospital; [2]Optometry Clinic, Mashhad University of Medical Sciences, Mashhad, Islamic Republic of Iran (Correspondence to M. Abrishami: abrishami.m@gmail.com).

Received: 16/03/05; accepted: 12/04/05

Introduction

Diabetes mellitus and its complications have confronted the developing as well as the industrialized world as a major public health problem. Despite being the leading cause of blindness in Americans between 20 and 64 years, the ocular complications of diabetes are preventable and treatable in the early stages of the disease [*1–3*]. Screening and monitoring programmes are agreed to be the most effective future means of minimizing the complications associated with diabetes mellitus. Besides the social benefits of living more years with adequate visual performance, there is a substantial cost saving by early detection of significant retinopathy using effective screening and monitoring methods [*4–7*]. Thus, a reliable, quick and inexpensive test for detection of early dysfunction is of vital importance to primary and shared care programmes.

Visual acuity charts only measure the high frequency component of the contrast sensitivity function and are markedly affected by small amounts of defocus [*8*]. Loss of low-frequency contrast sensitivity has been reported to reduce the ability to recognize faces and background images. It may also affect recognition of postures and movement [*9*]. Therefore, the contrast sensitivity function curve gives additional information about a subject's visual relationship to the environment and provides a more comprehensive description of visual performance than visual acuity alone. Visual acuity can be normal in some ocular diseases, including optic neuritis and glaucoma, where contrast sensitivity can be significantly decreased [*10,11*].

There is still controversy about the effectiveness of contrast sensitivity as a screening tool for diabetic retinopathy [*12–17*]. The present study investigated the use of Cambridge low-contrast grating as a potential screening tool for early detection of diabetic retinopathy by non-ophthalmologists, focusing on changes of low-contrast sensitivity in different stages of diabetic retinopathy.

Methods

This was a cross-sectional study of 95 patients with diabetes, referred to the ophthalmology clinic of Imam Reza General Hospital, Mashhad, Islamic Republic of Iran between May 2003 and August 2003. The study protocol was reviewed and approved by the ethics committee of the Research Assembly of Mashhad University of Medical Sciences.

The exclusion criteria were: significant ocular diseases beside diabetic retinopathy, including cataract, glaucoma, and optic nerve diseases, amblyopia, macular diseases, history of previous ocular surgery or photocoagulation and systemic diseases other than diabetes. After initial evaluations, 15 patients were excluded. Thus a total number of 154 eyes of 80 patients were evaluated.

For each patient, a questionnaire was completed about the type and duration of diabetes, mode of control and last blood glucose level, checked in the past month.

Objective refraction was done with a Topcon RM-A6500 autorefractometer and refined with manual retinoscopy (Hein HSR2) and axis refinement (Jackson cross-cylinder). Afterwards, the best corrected visual acuity was determined on a subjective basis. The visual acuity was checked with an illiterate E-chart. With the best correction of the refractive error, the contrast sensitivity was evaluated with a Cambridge low-contrast grating system. The test was done under a standard luminance of 100 cd/m^2, as described previously [*18*].

Table 1 **Background characteristics of diabetes patients with and without diabetic retinopathy**

Variable	No diabetic retinopathy	Diabetic retinopathy	Total
Age [mean (SD) years]	47.8 (15.3)	51.0 (9.3)	48.8 (13.8)
Sex (female%:male%)	69:31	75:25	70:30
Fasting blood sugar [mean (SD) mg/dL]	165.2 (47.7)	162.5 (46.7)	164.1 (47.7)
Diabetes duration [mean (SD) years]	6.2 (6.0)	11.8 (4.7)	8.0 (6.2)
Diabetes control (% of patients)			
Diet	3.8	0	2.6
Oral hypoglycemic agents	74.5	39.6	63.6
Insulin	21.7	52.1	31.2
Oral hypoglycemics + insulin	0	8.3	2.6

SD = standard deviation.

The chart luminance was regularly checked using a spot photometer. The visual acuity and contrast sensitivity were checked independently by an examiner who was blind to the results of other tests. Finally, slit-lamp evaluation of the anterior segment was used to exclude significant anterior segment pathology and narrowness of angle. Indirect ophthalmoscopy (fully-dilated) and non-contact slit lamp funduscopy were done by the same ophthalmologist.

As described by the Early Treatment Diabetic Retinopathy Study [*19*] the patients were classified as having no diabetic retinopathy, mild, moderate, severe, or very severe non-proliferative diabetic retinopathy (NPDR), early proliferative diabetic retinopathy (PDR), high-risk characteristic PDR (HRC-PDR), and/or clinically significant macular enema (CSME); the latter 2 were among the exclusion criteria.

Considering $P < 0.05$ significant, Pearson chi-squared, Student *t*-test and analysis of variance were used in analysing the relationships. A regression analysis was done to describe the correlation between visual acuity and Cambridge low-contrast grating measurements. *SPSS*, version 11.5 was used for all statistical calculations.

Results

The patients' characteristics are presented in Table 1. There was a statistically significant difference in the age of patients ($P = 0.031$) and duration of diabetes ($P < 0.0001$) for patients with and without diabetic retinopathy. Sex was not a significant determinant for diabetic retinopathy ($P < 0.50$).

Abnormal contrast sensitivity was observed in 27.1% of eyes with diabetic retinopathy, compared with 9.0% in unaffected eyes. The mean contrast sensitivity in the diabetic retinopathy group was 217.60 cps compared with a mean of 309.30 cps in the group without diabetic retinopathy (Tables 2 and 3). There was a statistically significant correlation between the presence of diabetic retinopathy and poor contrast sensitivity ($P < 0.01$). The contrast sensitivity deteriorated with more advanced diabetic

Table 2 **Cambridge low-contrast grating scores in diabetes patients with and without diabetic retinopathy, by sex**

Sex	No diabetic retinopathy Mean (SD) score	Diabetic retinopathy Mean (SD) score	Total Mean (SD) score
Male	314.2 (107.4)	244.16 (159.9)	295.1 (125.9)
Female	307.1 (116.6)	208.75 (151.1)	274.9 (136.3)
Total	309.3 (113.4)	217.60 (152.4)	280.7 (133.3)

P < *0.01.*
SD = standard deviation.

retinopathy (Table 4), but this was not statistically significant ($P = 0.349$, analysis of variance). However, there was a significant correlation between the duration of diabetes and the level of contrast sensitivity (Pearson $r = –0.216$, $P = 0.007$) (Figure 1).

There was a statistically significant correlation between the decrease in visual acuity and contrast sensitivity in eyes with diabetic retinopathy ($P = 0.049$) (Figure 2).

Discussion

After 20 years, almost 99% of patients with type 1 diabetes and 60% with type 2 diabetes will have some degree of diabetic retinopathy [*19*]. Beside the duration of disease, the age at onset is another important determinant of diabetic retinopathy: diabetic retinopathy is much more common in juvenile onset diabetes and this has major socioeconomic consequences. In one study, 86% of blindness in patients with a lower age of diabetes onset (age < 30 years) was attributable to diabetic retinopathy [*20*]. Prevention and interruption of this process depends on early detection and effective screening methods.

Table 3 **E-chart visual acuity in diabetes patients with and without diabetic retinopathy, by sex**

Sex	No diabetic retinopathy Mean (SD) score	Diabetic retinopathy Mean (SD) score	Total Mean (SD) score
Male	0.89 (0.12)	0.80 (0.26)	0.87 (0.17)
Female	0.88 (0.14)	0.78 (0.13)	0.83 (0.18)
Total	0.89 (0.14)	0.74 (0.21)	0.84 (0.17)

SD = standard deviation.

The success of any screening test obviously depends upon its ability to differentiate patients with the problem in question from other patients [*21*]. Regarding diabetic retinopathy, the ability of tests to differentiate those known to have diabetes mellitus but no retinopathy and those diabetes patients who have already developed diabetic retinopathy is of particular interest [*16*].

There is a marked controversy about the loss of contrast sensitivity in diabetes patients without retinopathy and the spatial frequencies at which losses occur in the presence of retinopathy. Early studies, such as that by Arden and Jacobson, used photographic plates to measure contrast sensitivity in diabetes patients with background diabetic retinopathy and another group with no retinopathy [*22*]. They found abnormal contrast sensitivity between normal and diabetes patients with background retinopa-

Table 4 **Contrast sensitivity and visual acuity according to the stage of diabetic retinopathy**

Stage of diabetic retinopathy	No. of patients	Contrast sensitivity Mean (SD) score	Visual acuity Mean (SD) score
Mild NPDR	19	275.3 (149.7)	0.77 (0.24)
Moderate NPDR	15	202.3 (151.9)	0.73 (0.19)
Severe NPDR	5	217.6 (165.9)	0.75 (0.00)
Very severe NPDR	5	233.0 (146.7)	0.60 (0.26)
Early PDR	5	57.0 (29.1)	0.76 (0.29)

SD = standard deviation.
NPDR = non-proliferative diabetic retinopathy; PDR = proliferative diabetic retinopathy.

thy, but there was no difference in contrast sensitivity between normal and diabetes patients without background retinopathy. Ghafour et al., using a similar method, also found that diabetes patients with background retinopathy had abnormal contrast sensitivity [*23*]. Unlike Arden and Jacobson, however, they reported that diabetes patients without retinopathy had abnormal contrast sensitivity at mid-frequencies.

Hyvarinen et al. measured individual contrast sensitivity functions in 19 patients with diabetes with different degrees of diabetic retinopathy [*24*]. They reported that patients with 20/20 acuity and background retinopathy showed abnormalities in con-

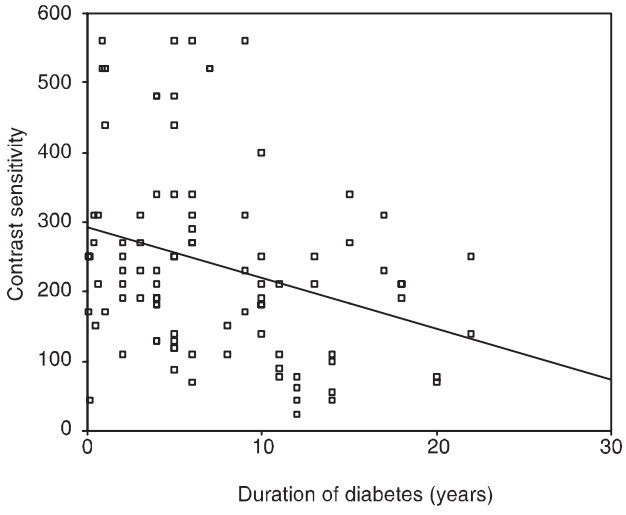

Figure 1 **Contrast sensitivity versus duration of diabetes mellitus**

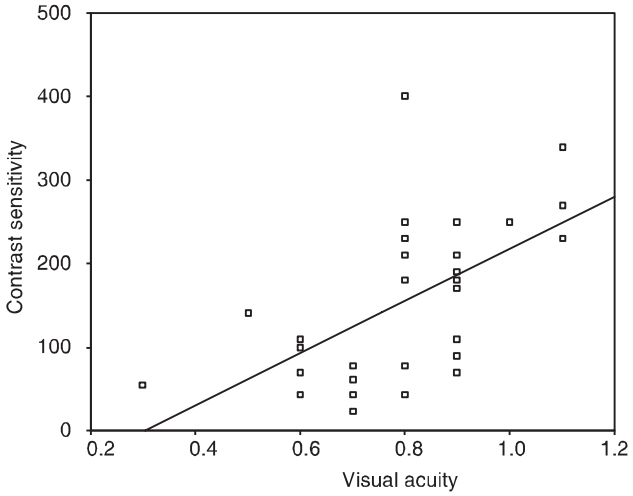

Figure 2 **Contrast sensitivity versus visual acuity in eyes with diabetic retinopathy**

trast sensitivity. They also suggested that contrast sensitivity fluctuates with blood sugar levels in diabetes, becoming reduced in the presence of hypoglycaemia.

Sokol et al. measured contrast sensitivity in type 1 and 2 diabetes patients with minimal or no diabetic retinopathy [*25*]. They found that type 2 diabetes patients with no retinopathy had abnormal contrast sensitivity at high spatial frequencies, while those with background diabetic retinopathy demonstrated abnormal contrast sensitivity at all tested spatial frequencies. Several authors found a significant loss of contrast sensitivity in early diabetic retinopathy groups at mid-to-high spatial frequencies using the Vistech VCTS chart [*14,26,27*]. Low-to-medium spatial frequency changes have also been reported to occur and it has been suggested that visual acuity measures alone may therefore be unreliable as a clinical indicator of loss of visual function [*28*].

To the best of our knowledge, this is the first study using Cambridge low-contrast grating in diabetic patients. We found a statistically significant difference in low spatial frequency contrast sensitivity between diabetics with and without retinopathy. This means that Cambridge low-frequency grating may be a potential screening tool for early retinopathic changes in diabetic patients.

There are a number of hypotheses about the potential causes of diminished contrast sensitivity in diabetic patients. Regan and Neima have reported a correlation between ischaemia of the parafoveal arcade using intravenous fluorescein angiograms and abnormal letter chart results [*12*]. This suggests that the pathophysiology responsible for contrast sensitivity loss in diabetes is due to functional loss of retinal ganglion cell dendrites, secondary to retinal ischaemia. Another factor, which may explain the etiology of reduced contrast sensitivity in diabetic eyes, is the diameter and extent of the foveal avascular zone [*1*]. Arend et al. found that the diameters of the foveal avascular zone and the perifoveal intercapillary area are significantly correlated with con-

trast sensitivity at mid-spatial frequencies [*29*]. Bresnick et al. revealed that the area of the foveal avascular zone in diabetics with non-proliferative diabetic retinopathy is significantly larger than healthy non-diabetic controls [*30*]. When the dimension of the foveal avascular zone progresses to greater than 1000 µm, visual acuity is usually diminished. This degree of destruction of the parafoveal capillary net is usually confined to cases of proliferative retinopathy. However, functional correlation of contrast sensitivity and foveal avascular zone extent is difficult because the diameter of the foveal avascular zone of a normal eye can vary considerably (350–750 µm) [*31*], and one cannot predict with accuracy the potential contrast sensitivity based solely on the appearance of the foveal avascular zone.

The rate of retinal blood flow may also affect the degree of contrast sensitivity loss. Several investigators have demonstrated enhanced retinal blood flow rates in diabetes patients with background retinopathy [*32–37*].

It is suggested that the diminished contrast sensitivity in diabetic patients is partially reversible by breathing oxygen, and is therefore probably the result of retinal hypoxia [*38*]. However, an improvement of contrast sensitivity does not occur after pan-retinal photocoagulation treatment, which implies that the reduction of contrast sensitivity is irreversible [*17*].

Conclusion

We found a significant diminution in contrast sensitivity in patients with early diabetic retinopathy compared with those without diabetic retinopathy. There was also a progressive deterioration of contrast sensitivity in more advanced stages of diabetic retinopathy. The findings are contrary to a number of previous studies, which found no statistically significant difference between diabetics without retinopathy and those with background retinopathy. This may be due to the use of a more sensitive tool in evaluation of contrast sensitivity in current study. It has been shown that the decrease in contrast sensitivity is more remarkable in low spatial frequencies. Hence, the Cambridge low frequency grating is a potential tool for the screening of early stages in diabetic retinopathy. However, larger, prospective studies will be needed to further investigate the sensitivity and specificity of the test as a screening tool.

Acknowledgements

We are indebted to the Research Assembly of the Mashhad University of Medical Sciences for its financial support of the project. Our sincerest thanks go to Ms Sherafat Javaheri for participation in performing the contrast sensitivity tests. We are also grateful to Dr H. Esmaili for his assistance in statistical analysis.

References

1. Flynn HW Jr, Smiddy WE, eds. *Diabetes and ocular disease: past, present, and future therapies.* San Francisco, American Academy of Ophthalmology, 2000 (Ophthalmology monograph 14).

2. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). United Kingdom Prospective Diabetes Study Group. *Lancet*, 1998, 352:837–53.

3. Tight blood pressure control and risk of macrovascular and microvascular com-

plications in type 2 diabetes: UKPDS 38. United Kingdom Prospective Diabetes Study Group. *British medical journal*, 1998, 317:703–13.

4. Early Treatment Diabetic Retinopathy Study Research Group. Results from the Early Treatment of Diabetic Retinopathy Study. *Ophthalmology*, 1991, 98:739–840.

5. Dasbach EJ et al. Cost–effectiveness of strategies for detecting diabetic retinopathy. *Medical care*, 1991, 29:20–39.

6. Javitt JC et al. Detecting and treating retinopathy in patients with type I diabetes mellitus. *Ophthalmology*, 1990, 97:483–93.

7. Cooke JB, Cochrane AL. A practical guide to low vision management of patients with diabetes. *Clinical & experimental optometry*, 2001, 84:155–61.

8. Bradley A et al. Effect of spherical and astigmatic defocus on acuity and contrast sensitivity: a comparison of three clinical charts. *Optometry and vision science*, 1991, 68:418–26.

9. Sekuler R, Hutman LP, Owsley CJ. Human ageing and spatial vision. *Science*, 1980, 209:1255–6.

10. Zimmern RL, Campbell FW, Wilkinson IMS. Subtle disturbances of vision after optic neuritis elicited by studying contrast sensitivity. *Journal of neurology, neurosurgery, and psychiatry*, 1979, 42:407–12.

11. Ross JE, Bron AJ, Clarke DD. Contrast sensitivity and visual disability in chronic simple glaucoma. *British journal of ophthalmology*, 1984, 68:821–7.

12. Regan D, Neima D. Low contrast letter charts in early diabetic retinopathy, ocular hypertension, glaucoma, and Parkinson's disease. *British journal of ophthalmology*, 1984, 68:885–9.

13. Della Sala S et al. Impaired contrast sensitivity in diabetic patients with and without retinopathy. A new technique for rapid assessment. *British journal of ophthalmology*, 1985, 69:136–42.

14. Trick GL et al. The relationship between hue discrimination and contrast sensitivity deficits in patients with diabetes mellitus. *Ophthalmology*, 1988, 95:693–8.

15. Khosla PK, Talwar D, Tewaari HK. Contrast sensitivity changes in background diabetic retinopathy. *Canadian journal of ophthalmology*, 1991, 26:7–11.

16. Ismail GM, Whitaker D. Early detection of changes in visual function in diabetes mellitus. *Ophthalmic & physiological optics*, 1998, 18:3–12.

17. Mackie SW, Walsh G. Contrast and glare sensitivity in diabetic patients with and without pan-retinal photocoagulation. *Ophthalmic & physiological optics*, 1998, 18:173–81.

18. Jones HS, Moseley MJ, Thompson JR. Reliability of the Cambridge low contrast gratings. *Ophthalmic & physiological optics*, 1994, 14(3):287–9.

19. *Retina and vitreous, Section 9. Basic and clinical science course.* San Francisco, American Academy of Ophthalmology, 2004/05:99–119.

20. Klein R et al. The Wisconsin Epidemiologic Study of Diabetic Retinopathy. II. Prevalence and risk factors of diabetic retinopathy when age at diagnosis is less than 30 years. *Archives of ophthalmology*, 1984, 102:520–6.

21. Ivers RQ et al. Sensitivity and specificity of tests to detect eye disease in an older population. *Ophthalmology*, 2001, 108:968–75.

22. Arden GB, Jacobson JJ. A simple grating test for contrast sensitivity: preliminary results indicate value in screening for

glaucoma. *Investigative ophthalmology & visual science*, 1978, 17:23–5.

23. Ghafour IM et al. Contrast sensitivity in diabetic subjects with and without retinopathy. *British journal of ophthalmology*, 1982, 66:492–5.

24. Hyvarinen L, Laurinen P, Rovamo J. Contrast sensitivity in evaluation of visual impairment due to diabetes. *Acta ophthalmologica*, 1983, 61:94–101.

25. Sokol S et al. Contrast sensitivity in diabetics with and without background retinopathy. *Archives of ophthalmology*, 1985, 103:51–4.

26. Banford D et al. Longitudinal study of visual functions in young insulin dependent diabetics. *Ophthalmic & physiological optics*, 1994, 14:339–46.

27. Bangstad HJ et al. Impaired contrast sensitivity in adolescents and young type 1 (insulin-dependent) diabetic patients with microalbuminuria. *Acta ophthalmologica*, 1994, 72:668–73.

28. Di Leo MA et al. Presence and further development of retinal dysfunction after 3-year follow up in IDDM patients without angiographically documented vasculopathy. *Diabetologia*, 1994, 37:911–6.

29. Arend O et al. Contrast sensitivity loss is coupled with capillary dropout in patients with diabetes. *Investigative ophthalmology & visual science*, 1997, 38:1819–24.

30. Bresnick GH et al. Abnormalities of the foveal avascular zone in diabetic retinopathy. *Archives of ophthalmology*, 1984, 102:1086–293.

31. Sleightholm MA, Arnold J, Kohner EM. Diabetic retinopathy: 1. The measurement of intercapillary area in normal retinal angiograms. *Journal of diabetic complications*, 1988, 11:113–6.

32. Kohner EM. Problems of retinal blood flow in diabetes. *Diabetes*, 1976, 25:839–44.

33. Soeldner JS, Christacopulos PD, Gleason RE. Mean retinal circulation time as determined by fluorescein angiography in normal prediabetic and chemical-diabetic subjects. *Diabetes*, 1976, 25:903–8.

34. Findl O et al. Ocular haemodynamics and colour contrast sensitivity in patients with type 1 diabetes. *British journal of ophthalmology*, 2000, 84:493–8.

35. Sinclair SH et al. Retinal vascular autoregulation in diabetes mellitus. *Ophthalmology*, 1982, 89:748–50.

36. Fallon TJ, Chowiencyzk P, Kohner EM. Measurement of retinal blood flow in diabetics by blue-light entoptic phenomenon. *British journal of ophthalmology*, 1986, 70:43–6.

37. Rand LI et al. Multiple factors in the prediction of risk of proliferative diabetic retinopathy. *New England journal of medicine*, 1985, 313:1433–8.

38. Arden GB, Wolf JE, Tsang Y. Does dark adaptation exacerbate diabetic retinopathy? Evidence and a linking hypothesis. *Vision research*, 1998, 38:1723–9.