Impaired motion sensitivity as a predictor of subsequent field loss in glaucoma suspects: the Roscommon Glaucoma Study

J Wu, M Coffey, A Reidy, R Wormald

Abstract

Aim—To determine if impaired motion sensitivity is a significant predictor of subsequent field loss in glaucoma suspects.

Method—A population based prospective study; a 5 year follow up of all glaucoma suspects who had been identified from a population based random sample survey in the west of Ireland. 78 glaucoma suspects whose visual field function was annually measured by Henson CFS 2000 and for whom data on family history of glaucoma, ocular status, and motion impairment had been recorded. Visual field loss was defined as Henson visual field survival score of 94 or less.

Results—18 people developed visual field loss in at least one eye. Motion impairment at baseline was associated with a 2–18 times greater risk of development of the visual field loss ($p < 0.001$). This association was independent of sex, family history of glaucoma, intraocular pressure, and C/D ratio at baseline. The Cox's proportional hazards regression analysis confirmed the above results after adjustment for age and the C/D ratio.

Conclusion—Motion impairment is an independent predictor of visual field loss in glaucoma suspects, although it is not clear how long motion impairment precedes visual field loss.

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relation between motion impairment and visual field loss in all glaucoma suspects who were detected from a population based random sample survey in county Roscommon, the west of Ireland.⁸

Method

STUDY DESIGN

This study is a 5 year prospective study; annual follow up of all glaucoma suspects who had been detected during the Roscommon Glaucoma Survey between 1989 to 1990.⁸ The ethics committee of the Western Health Board reviewed and approved the study. Informed consent for participation in the study was obtained from all subjects before their enrolment.

DEFINITIONS

Normal visual field—Henson visual field survival score was greater than 94. This cut off was used to define the field in the survey.⁸

Glaucoma suspect—Normal visual field, with intraocular pressure (IOP) greater than 21 mm Hg, or with abnormal cup/disc (C/D) ratio (C/D > 0.5, difference of C/D ratio between two eyes > 0.2).

Visual field loss (end point)—During the follow up, the Henson visual field survival score was 94 or less.

Motion impairment (exposure measurement)—Motion detection score was less than 86%.

Age—Defined as age at entering the study.

STUDY POPULATION

All glaucoma suspects from the Roscommon Glaucoma Survey were recruited. The methods of selection of population in the survey have already been described.⁸ Briefly, 2200 people aged 50 and over in County Roscommon, in the west of Ireland, were randomly sampled from the electoral register of the Republic of Ireland, using the Ran-Sam programme. The attendance rate in the survey was 99.5%.

MEASUREMENT INSTRUMENTS

The visual field test (Henson CFS2000, 132 points; Keeler Inc 1989) is a type of semiautomated, suprathreshold perimetry to detect the intensity of brightness to be seen within the central 24 degrees of the visual field. It presents multiflashes to the patient in patterns of 2, 3, or 4 at a time. The patient indicates how many points or "flashes" are seen at each presentation and localises their positions when it is required. To complete a test takes 3–8 minutes.

Southampton
University Ophthalmic
Epidemiology Unit

J Wu
A Reidy

Western Health Board
(Ireland)
M Coffey

Glaxo Department of
Ophthalmic
Epidemiology,
Moorfields Eye
Hospital, London
R Wormald

Correspondence to:
J X Wu, Eye Unit,
Southampton General
Hospital, Tremona Road,
Southampton SO16 6YD.

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Based on histological examinations,¹ it is reported that a selectively greater loss of large nerve fibres had been observed in the early stage of glaucoma.^{1,2} Clinically, this corresponds with difficulty in seeing motion or flicker in the early stage of the disease. Because current standard perimetry does not measure motion or flicker function, large nerve fibre damage such as is found in patients with glaucoma may be undetected.³

A number of clinical observations have provided support for this hypothesis. Several cross sectional studies have demonstrated motion impairment in glaucoma suspects.⁴⁻⁷ The main limitation of these studies is the lack of clarity of the exposure-disease relation in time. They are unable to demonstrate whether an abnormal result of the new test is an early detection.

The aim of this study was to determine if there was motion impairment before frank visual field loss in early glaucoma. The objective of the study was to investigate the

The initial intensity of the flashes is settled 5 dB above a threshold at which approximately 50% flashes could be seen. The test provides a survival score of visual field (ranged from $-\infty$ to 100).⁹ The survival score of more than 95 was regarded as normal visual field.

The Motion Test (Motion Sensitivity Perimetry, Version 5, Institute of Ophthalmology, London, 1990) was specifically designed for measuring motion impairment within the central 21 degrees of the visual field.¹⁰ The moving stimuli were vertical bars as described in detail by Fitzke *et al*.⁴ and the observer was asked to press a response button when any movement was detected on the display. The area of motion stimulus varied between 3 mm² to 6 mm² as a function of eccentricity. The Michelson contrast was 58.8% with a white colour. The stimulus (bar) moved from side to side for a 0.2 second period. The test randomly examined 16 locations with one displacement distance (amplitude) and then the procedure was repeated five times. The amplitude varied according to the eccentricity of stimulus. Therefore, the amplitude tested in eccentricity of 3, 9, 15, to 21 is 10, 9.8, 9.6, and 9.1 min arc, respectively. The viewing distance was equivalent to the diagonal distance of the computer display (12 inch). To complete a motion test took 5–8 minutes, based on subjects' response times and the number of defects. Motion sensitivity score was based on the percentage of response from a total of 84 movements over 14 locations (excluding two close points to the blind spot). The test was done in the same room as the Henson visual field test.

INCLUSION CRITERIA

There were 88 glaucoma suspects detected from the survey.⁸ Out of them, 78 subjects fulfilled all of the following inclusion criteria:

- 1 Had the motion test at beginning of the study
- 2 Records of ocular examinations in the survey
- 3 Visual acuity 6/18 or better at baseline
- 4 Normal Henson visual field at baseline.

EXAMINATION PROCEDURE

The study was conducted during 1990–6.

Baseline

During the survey, a comprehensive ocular examination was performed by two ophthalmologists (MC, RW), including following tests: the best corrected visual acuity using 6 metre Snellen chart, Goldmann tonometer or Perkins Mk2 hand held applanation tonometer, and optic disc ratio assessment using slit lamp biomicroscope with the van Herick method. Two operators carried out the visual field test and the motion test.

Follow up

Visual field follow up examination was carried out by an ophthalmologist (MC), who was one of two government appointed community ophthalmologists to the county. The results of motion tests were not disclosed to the ophthalmologist during the period of the study. A mobile ophthalmic unit was used to visit glaucoma suspects throughout the county.

The length of the follow up was defined as the time from baseline examination to final visit for those who did not have visual field loss or from the baseline to the time when the visual field loss was first detected.

Sixty eight (87.2%) out of the 78 subjects completed a visual field test at the fifth year. The median period of follow up was 5 years (range 1–5).

DATA ANALYSIS

The baseline factors studied included age, sex, occupation, family history, visual acuity, IOP, C/D ratio, and visual field. These were selected on the basis of other published work. Clinical data were always collected from two eyes for each person when it was possible. For data analysis, one eye per person was used, taking the eye in the worse C/D ratio. For those patients in whom the ratio in both eyes were equal, one eye was recruited randomly for inclusion. All subjects were white Europeans.

χ^2 Tests were performed to investigate potential associations between the motion impairment and other baseline measurements. Where appropriate, Fisher's exact test was used. Cox's proportional hazards regression models were used to determine the motion impairment as an independent predictor of visual field loss, accounting for associations with various baseline factors and the variable length of follow up. Patients with inadequate period of follow up (1 year or less) were excluded from analysis. The results are presented as relative risks (hazard ratios with 95% confidence intervals). Test statistics were interpreted in a two tailed fashion. Data were double entered onto a computer and analysed using the software package SPSS and STATA (Stata Corporation Version 5.0).

Results

POPULATION OF GLAUCOMA SUSPECTS

The study sample comprised 78 glaucoma suspects. Approximately half had IOP greater than 21 mm Hg alone; more than one third had abnormal C/D ratio; and 14% had a combination of both abnormal IOP and C/D ratio (Table 1). There were seven cases with a family history of glaucoma. The mean age was 64.5 (SD 9.16) years.

ASSOCIATIONS WITH THE MOTION IMPAIRMENT

Overall, there were 27 (34.6%) with motion impairment. The motion impairment (Table 2) was not significantly associated with sex, occu-

Table 1 Clinical characteristics of 78 glaucoma suspects

Glaucoma suspects		n	%
I	IOP >21 mm Hg only	38	48.7
II	C/D ratio >0.5 or C/D difference between two eyes >0.1	29	37.2
III	I+II	11	14.1
Total		78	100

Table 2 Baseline characteristics of the two cohorts

Characteristics	Motion impairment		Normal motion		Total No of subjects	χ^2 test p Value
	No	%	No	%		
Age (years):						
50–59	2	7	25	49	27	
60–69	8	30	16	31	24	
≥70	17	63	10	20	27	<0.001
Sex:						
Male	10	37	27	53	37	
Female	17	63	24	47	41	0.18
Occupation:						
Farmer	22	81	37	73	59	
Non-farmer	5	19	14	27	19	0.38*
Family history:						
No	26	96	45	88	71	
Yes	1	4	6	12	7	0.23*
Visual acuity:						
6/6–6/9	18	68	35	69	53	
6/12–6/18	9	32	16	31	25	0.86
IOP:						
<21 mm Hg	12	44	17	33	29	
>21 mm Hg	15	56	34	67	49	0.46
C/D:						
Normal	9	33	29	57	38	
Abnormal	18	67	22	43	40	0.059

*Fisher's exact test.

Table 3 Relative risk (RR) for visual field loss by motion impairment using crude 5 year cumulative incidence

Motion impairment	No of patients	Visual field 5 years cumulative loss	RR (95% CI)	p Value
No (>85%)	51	4 (7.8%)		
Yes (≤85%)	27	14 (52%)	6.6 (2.41 to 18.13)	<0.001

Table 4 Independent predictor of visual field loss (95% confidence interval (CI)), using Cox proportional hazards regression analysis

Motion impairment	Visual field loss (n=18)	Rate ratio (95% CI)	Rate ratio adjusted for age (95% CI)	Rate ratio adjusted age, IOP and C/D (95% CI)
No (>85%)	4	1.0	1.0	1.0
Yes (≤85%)	14	8.36 (2.75 to 25.4)	6.31 (1.88 to 21.68)	4.11 (1.26 to 13.5)

pation, family history, visual acuity, IOP, and C/D ratio, but there was a statistically significant association with age ($p<0.001$).

VISUAL FIELD LOSS

During the 5 years of annual visual field follow up 18 (23%) patients developed visual field loss. Five patients had visual field loss in both eyes but only one had visual field loss in both eyes on the same visit. Among people who developed the visual field loss, 14 (78%) had motion impairment initially. An unadjusted relative risk of the visual field loss was approximately seven times greater among those with the motion impairment than those without such impairment (Table 3). The Cox unadjusted RR was 8.36 (95 CI 2.75 to 25.4) (Table 4). Relative risk was not significantly altered after adjustment for age.

Discussion

BIAS

One source of the selection biases is caused by loss of subjects to follow up. With the mobile unit carrying out follow up examinations, a follow up rate of 85% was reached. Because a high attendance and follow up rate were achieved selection bias was generally minimised. However, there is evidence that people who were lost to follow ups were older than

those people who were followed up ($p=0.04$). The reasons for non-participation were death ($n=2$), sickness ($n=4$), or the inability to complete visual field tests ($n=3$). There is no evidence that motion impairment in the loss of the follow ups differed from people who were completely followed.

Since the investigator (MC) was not aware of the results of the motion sensitivity during the follow up, the testing procedure did not differ according to the motion impairment. Observer bias from interpreting test was also eliminated with the motion test and the visual field test since both instruments produce a digital read-out. However, there was a lack of information to interpret the score correctly at the stage of data analysis because the motion test was a prototype. Based on several previous clinical observations^{4–7} an empirical cut off point (85%) was deliberately chosen to ensure a high sensitivity for detecting motion impairment. If the cut off level is too sensitive, it is possible that some false positives from the motion test may occur. In addition, taking only one measurement of the motion test (as was done in this study), is also likely to add some misclassification of motion impairment. This is because there was a certain degree of random within person variability of the test.^{10 11}

Although these observer biases did not differ according to the exposure or outcome measurements, since the measurements were automatically taken or the exposure was blind to the investigator, a certain amount of non-differential misclassification could happen. This could dilute estimating the association between the motion impairment and the visual field loss, and therefore the predictive value of motion sensitivity may be underestimated.

PREDICTOR OF THE VISUAL FIELD LOSS

There is little doubt that a proportion of glaucoma suspects have some motion impairment. This is demonstrated by both previous studies^{4–7} and by the current study. All the previous studies, however, have been based on cross sectional studies. They are subject to one important limitation; a cross sectional study can not clearly establish the temporal association between the motion impairment and the visual field loss.

The current study investigates whether motion impairments precede visual field loss in glaucoma suspects. These data show that motion impairment is a strong predictor of visual field loss. Among the subjects with no visual field loss, 22% had motion impairment at the baseline. Although visual field abnormalities in some subjects did not meet the definition of visual field loss, there is evidence that such eyes may proceed to develop visual field loss. Approximately half of these eyes (6/13) had shown that the cup disc ratio was 0.6 or greater which is highly correlated with the future development of visual field loss.^{12–14}

Four subjects with normal motion sensitivity had the visual field loss during the follow up. There was no evidence to show any clinical pattern from them. For this group, it is difficult to establish whether these subjects have different

mechanisms of visual field loss from the majority of glaucoma patients. Several studies have also suggested that it could be the case that some glaucoma patients can have small nerve fibre damage preceding the large nerve fibre damage.^{15 16} In such cases the motion impairment may not precede a visual field loss.

EYE OR INDIVIDUAL

Even though glaucomatous damage often begins asymmetrically in one eye, eventually the patient is affected bilaterally. It is therefore inappropriate to treat one eye as an independent unit, especially in assessing associations between risk factors and outcomes. For such reason the authors have treated a person as the unit of analysis and have chosen the worse eye when both eyes had different ophthalmic results. One of the advantages of this approach is that it is simple and interpretable.^{17 18} One of the disadvantages could be to underestimate the association of interests. For instance, it is not possible to adjust for the fact that those people with motion impairment are more likely to have visual field loss in both eyes at the same visit or to have the visual field loss in one eye first, followed by the other in a very short period, than those without the motion impairment.

SELECTIVE VISUAL FUNCTION DAMAGE

Quigley and colleagues' findings that early light sensitivity loss cannot be found unless the defect is at least 5 dB, or when more than 20% of the total ganglion cell fibres have been lost,^{1 3} suggests that a 4 dB sensitivity loss corresponds to a 10% cell death. The 10% ganglion cell death could mean very little if it is compared with large variation in the total ganglion cell population in normal individuals.¹⁹ Supposing the 10% cell death was in predominantly large ganglion cells, then there would be a substantial motion function loss.²⁰ By analogy, it would be expected that large ganglion cell function damage would be detected more efficiently than small ganglion cell function damage. In addition, because large ganglion cell damage may be more likely to affect perception of motion and high temporal frequency flicker,²¹ our finding supports the above hypothesis that glaucoma could have selective vision damage at an early stage.

Conclusion

The authors believe this is the first time that a study related to motion sensitivity test has recruited glaucoma suspects representative of those in the general population and followed them for 5 years. In this study, glaucoma suspects were selected based on a *broad* definition and provided representative samples from a population based study.

These data provide the first reported evidence that motion impairment precedes visual

field loss and supports the hypothesis that a majority of early glaucoma patients may have large nerve fibre damage before they suffer damage to the small nerve fibre. Future studies in this area will need to show by how long motion impairment precedes visual field loss.

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- 1 Quigley HA, Sanchez RM, Dunkelberger GR, *et al*. Chronic glaucoma selectively damages large optic nerve fibers. *Invest Ophthalmol Vis Sci* 1987;28:913-20.
- 2 Quigley HA, Coleman AL, Dorman Pease ME. Larger optic nerve heads have more nerve fibers in normal monkey eyes. *Arch Ophthalmol* 1991;109:1441-3.
- 3 Quigley HA, Dunkelberger GR, Green WR. Retinal ganglion cell atrophy correlated with automated perimetry in human eyes with glaucoma. *Am J Ophthalmol* 1989;107:453-64.
- 4 Fitzke FW, Poinsoosawmy D, Ernst W, *et al*. Peripheral displacement thresholds in normals, ocular hypertensive and glaucoma. In: Greve EL, Heijl A eds. *Seventh International Visual Field Symposium*. Dordrecht: Martinus Nijhoff/Dr W Junk Publishers 1986:447-52.
- 5 Silverman SE, Trick GL, Hart WM. Motion perception is abnormal in primary open-angle glaucoma and ocular hypertension. *Invest Ophthalmol Vis Sci* 1990;31:722-9.
- 6 Trick GL. Retinal potentials in patients with primary open-angle glaucoma: physiological evidence for temporal frequency tuning deficits. *Invest Ophthalmol Vis Sci* 1985;26:1750-8.
- 7 Wu J. Visual screening for blinding diseases in the community using computer controlled video perimetry. PhD thesis. London: University of London, 1993.
- 8 Coffey M, Reidy A, Wormald R, *et al*. Prevalence of glaucoma in the west of Ireland. *Br J Ophthalmol* 1993;77:17-21.
- 9 Henson-DB. Visual field screening and the development of a new screening program. *J Am Optom Assoc* 1989;60:893-8.
- 10 Wu J, Jones B, Brown A, *et al*. Preliminary report of the use of laptop computer perimetry with a motion sensitivity test to detect optic nerve disease in rural West Africa. In: Mills RP, ed. *Perimetry Update*. Amsterdam/New York: Kugler Publications, 1992/1993:323-9.
- 11 Wu J, Wormald R, Fitzke F, *et al*. Laptop computer perimetry for glaucoma screening. *Invest Ophthalmol Vis Sci* (Suppl) 1991;32:810.
- 12 Armaly MF, Krueger DE, Maund L, *et al*. Biostatistical analysis of the collaborative glaucoma study. I. Summary report of the risk factors for glaucomatous visual-field defects. *Arch Ophthalmol* 1980;98:2163-71.
- 13 Damms T, Dannheim F. Sensitivity and specificity of optic disc parameters in chronic glaucoma. *Invest Ophthalmol Vis Sci* 1993;34:2246-50.
- 14 Jonas JB, Gusek GC, Naumann GO. Optic disc morphometry in chronic primary open-angle glaucoma. II Correlation of the intrapapillary morphometric data to visual field indices. *Graefes Arch Clin Exp Ophthalmol* 1988;226:531-8.
- 15 Johnson CA, Adams AJ, Casson EJ, *et al*. Progression of early glaucomatous visual field loss as detected by blue-on-yellow and standard white-on-white automated perimetry. *Arch Ophthalmol* 1993;111:651-6.
- 16 Johnson CA, Brandt JD, Khong AM, *et al*. Short-wavelength automated perimetry in low-, medium-, and high-risk ocular hypertensive eyes. Initial baseline results. *Arch Ophthalmol* 1995;113:70-6.
- 17 Glynn RJ, Rosner B. Accounting for the correlation between fellow eyes in regression analysis. *Arch Ophthalmol* 1992;110:381-7.
- 18 Glynn RJ, Buring JE. Ways of measuring rates of recurrent events. *BMJ* 1996;312:364-7.
- 19 Devaney KO, Johnson HA. Neuron loss in the aging visual cortex of man. *J Gerontol* 1980;35:836-41.
- 20 Leaventhal AG, Rodieck RW, Dreher B. Retinal ganglion cell classes in the Old World monkey: morphology and central projections. *Science* 1981;213:1139-42.
- 21 Livingston MS, Hubel DH. Psychophysical evidence for separate channels for the perception of form, color, movement, and depth. *J Neurosci* 1987;7:3416-6.