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Employing following eye movements to discriminate normal from glaucoma subjects

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ABSTRACT

We recorded optokinetic nystagmus (OKN) to see if slow phase velocity, duration or other measures were affected by glaucoma. Drifting grating patterns that either weakly or strongly evoked the spatial frequency doubling illusion were employed. Analysis of 68 variables characterizing the OKN revealed that small subsets of these variables were good at discriminating normal from primary open angle glaucoma subjects. The variables were related to the regularity of following eye movements. Models including the best five variables selected in two different ways classified about 90% of subjects correctly. Impaired accuracy of eye movements suggests that glaucoma changes the signal to noise ratio available to the brain. The gross changes observed permit the use of electro-oculography or other simple methods in the clinic.

Key words: frequency doubling, glaucoma, illusion, optokinetic nystagmus, variability.

INTRODUCTION

Optokinetic nystagmus (OKN) is driven by two components: the direct 'fast' pathway and the indirect 'slow' pathway containing the velocity storage mechanism. Studies of the nucleus of the optic tract (NOT) implicate it in OKN control.^{2,3} In higher mammals, neurons of the NOT receive input from the visual cortex,⁴ and thereby receive input from larger retinal ganglion cell types (M cells). Since M cells are thought to be selectively damaged by glaucoma,⁵ it might also be proposed that primate OKN is affected by glaucoma.

In glaucoma the OKN system may try to compensate for reduced visual input by increasing OKN gain, but gain

changes cannot ameliorate declining signal-to-noise ratios associated with declining ganglion cell numbers. Recent work shows that even large well-defined human OKN slow phase velocities can be rapidly changed, consistent with fast pathway dominated input.^{6,7} Thus, declining signal-to-noise ratios associated with M-cell death in glaucoma might translate into rapidly fluctuating OKN slow phase velocities, even in easily measured large contiguous beats. Given the relative success of tests for glaucoma using the spatial frequency doubling (FD) illusion,⁸⁻¹⁰ and its links to the M cells,¹¹ we decided to examine OKN slow phase behaviour in response to drifting patterns using FD and near-FD stimuli.

METHODS

Measurements were made for four different stimuli (Table 1) described by the equation:

$$L(x,t) = L_m (1 + C * T(ft) * \sin(2\pi(sx - dt))),$$

where L_m is the background intensity, C the contrast, f is the temporal modulation rate of the contrast, s is the spatial frequency, and d is the temporal frequency of grating drift. $T(ft)$ was a square wave at 27.2 Hz or 0 Hz. In all cases s was 0.25 c/deg and d was 6.79 Hz. The video monitor ($L_v = 52 \text{ cd/m}^2$) subtended 31.4 deg horizontally and 27.7 deg vertically. The previously described subjects² consisted of two groups of roughly age-matched normal controls ($N = 10$) and a test group consisting of primary open angle glaucoma (POAG) suspects ($N = 8$). Subjects had clear ocular media, vertical cup to disc ratios of 0.6 or greater, and a highest recorded intraocular pressure of 20 mmHg or greater. Right eyes were tested. Eye position, recording and analysis were performed as previously described.⁷ All subjects gave informed written consent.

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Commercial interest T Maddess holds a patent on the optokinetic nystagmus following eye movements method. The results of this paper could be construed as supporting the basis for this method.

Table 1

Test	T(ft) (Hz)	, Contrast	Drift direction
1	27.2	0.6	Left to right
2	27.2	0.6	Right to left
3	0	0.4	Left to right
4	0	0.4	Right to left

Table 2

Vat-table	Description
TVV	Total variation in OKN slow phase velocity (V)
$RTV_{wf}V$	Relative total variation in OKN slow phase velocities well fit by a straight line
SDV	Standard deviation in the OKN slow phase velocity (V)
SDT	Standard deviation in the OKN beat duration (T)
$SD_{wf}T$	Standard deviation in OKN beat duration (T) for beats whose slow phase well fit a straight line
$M_{wf}T$	Mean OKN beat duration for those OKN beats whose slow phase was well fit by a straight line
MR	Mean rate of OKN beats
$M_{cl}R$	Mean rate of OKN beats occurring within contiguous clusters
$M_{cl}S$	Mean eye deflection in degrees (Size, S) per OKN beats occurring within contiguous clusters
$M_{clwf}T$	Mean duration (T) of those OKN beats occurring within contiguous clusters of beats and whose slow phase was well fit by a straight line

OKN, optokinetic nystagmus

Analysis of eye position identified individual OKN beats and their position in the eye movement record (approximately 2 min of OKN activity). In our records, contiguous OKN beats were said to be 'clustered (cl) while periods without contiguous beats were called 'gaps'. Slow phase beats were further classified as being 'well fit' (wf) by straight lines ($r^2 > 0.85$) or not. Variables examined included the median, mean and standard deviation in OKN slow phase duration, size (deflection in degrees), velocity, rate and gap duration. Total variation (TVV) in OKN slow phase velocity, and relative total variation (RTV) were also examined where $TVV = \sum |v_i - v_{i+1}| v_i$ being, for example, the i^{th} slow phase velocity in the eye position record. $RTV = TVV / SDS$ where SDS is the standard deviation in the OKN beat size. The resulting 68 parameters from each test record were subjected to a stepwise discriminant analysis using SPSS to ascertain whether some combination of parameters could reliably discriminate between the normal and the test group. The variables were included in the discriminant analysis according an F-test criteria (SPSS, MaxMinF), and variables were excluded or included over several iterations. Table 2 defines the variable names presented in Table 3. For example, the parameter $SD_{wf}T_1$ is the standard deviation of those OKN durations (T) that had slow phases well fit (wf) by straight lines for test stimulus 1.

Table 3.

Selectton	Variables	Normal	Test	Correct
All variables	SDV, SDV, $RTV_{wf}V_3$, $RTV_{wf}V_4$, $M_{cl}R_1$, $SD_{cl}T_4$, SDT, $M_{cl}S_2$, $M_{wf}T_3$, $SD_{wf}T_2$, $M_{clwf}T_2$	100%	100%	100%
Best 5 FD	$M_{clwf}T_2$, SDT ₂ , $M_{cl}S_2$, $M_{cl}R_1$, SDV, (or TVV ₁)	85.7%	90.0%	88.2%
Best 5 No OKN duration	MR, MR, $M_{cl}R_4$, SDV, $RTV_{wf}V_4$	87.5%	100%	94.7%

RESULTS

The initial analysis included the variables from all four test stimuli. Of the selected 11 variables (row 1 of Table 3), seven were concerned with the standard deviation or relative total variation of OKN parameters, and five were concerned with well fit and/or clustered OKN beats. Variables from FD (Test 1 and 2) and near-FD (Tests 3 and 4) stimuli were approximately equally well represented. Variables associated with gaps were never important. It is not surprising that 11 variables could achieve good discrimination so we examined smaller sets of five potentially interesting variables.

In the first instance, the analysis was restricted to variables from FD tests. The best performing discriminant model formed from five FD variables (row 2 of Table 3) were assessed (discriminant models including SDV, and TVV, performed equally well). Again, variables associated with clustered and well fit OKN beats and the variation of beat velocity were selected, providing 88.2% correct diagnosis. Two of the variables had to do with OKN duration (e.g. $M_{clwf}T_2$). Variables associated with duration were significantly ($P < 0.05$) correlated with subject age. To obtain a less age-dependent discrimination we excluded duration-based variables. The new discriminant analysis produced five new variables (row 3 of Table 3) that were concerned with OKN rate and variation, but only for the near-FD stimuli (tests 3 and 4). Figure 1 shows the mean values of the four most interesting variable types and their standard deviations

DISCUSSION

Good discrimination between the normal and glaucoma test groups was obtained. The figure of approximately 90% correct diagnoses is impressive, given that the eyes were simply POAG suspects. Most of the variables selected by stepwise discriminant analysis were associated either with

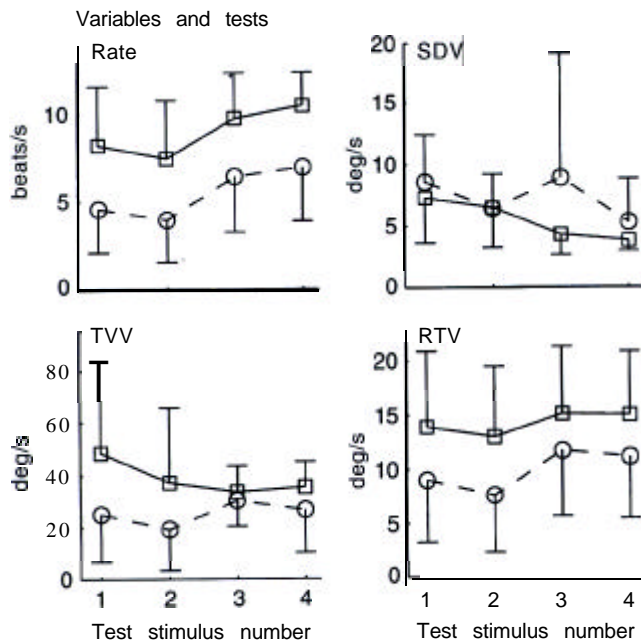


Figure 1. Means and standard deviations of interesting variables from Table 2. Test numbers as in Table 1.

OKN beat rate, or with variations in the slope of well-defined OKN slow phases (i.e. well fit by straight lines, occurring in contiguous clusters). As shown in Fig. 1, the distributions of variables associated with the FD stimuli were somewhat better separated than those for the non-FD

stimuli. Nevertheless, near-FD stimuli produced the least age-dependent and most accurate results.

The fact that large, contiguous OKN beats are useful for diagnosis is encouraging from the perspective of clinical utility, since these are readily observable with electro-oculograms (EOG). If following eye movements that were more rambling and/or smaller proved diagnostic, this would have posed a signal detection problem. The OKN method (Australia Patent no. 645420 (1994a), held by TM) also provides an alternative to attempting to find a contrast threshold using eye movements in cases where small OKN beats would again cause a detection problem. The use of frequency doubling stimuli, by virtue of their low spatial frequencies, mean that subjects need not be particularly well refracted.

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