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Parallel pathways, noise masking and glaucoma detection: behavioral and electrophysiological measures

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Abstract. Purpose: We tested the hypothesis that because of their reduced neural efficiency, glaucoma patients should have increasingly impaired thresholds as external noise is added to a stimulus. Method: We compared the performance of 20 normals (mean age = 39 years) with that of 15 patients with early glaucoma or at very high risk for glaucoma (mean age 45 years). All patients had normal visual acuity. Contrast thresholds were measured on two sets of tasks: (1) behavioral and (2) sweep visually evoked potentials (VEPs). Two stimuli were used (a) 7.5 Hz reversing gratings of 0.69 cpd, and (b) 5.5 cpd gratings. Noise was binary and contrast varied from 0 to 80%. Psychophysical thresholds were determined using a staircase which employed a spatial four alternative forced choice procedure (4AFC) and converged on 50% correct. Sweep VEP thresholds were determined by extrapolation to zero volts as a function of log contrast. Results: Differences between normal subjects and patients with early glaucoma were not significant without noise. Both the absolute size of the difference and its significance increased as noise level increased. For the behavioral thresholds these trends were clearer with the 5.5 cpd grating, while for the sweep VEPs they were more clear for the 0.69 cpd grating. Conclusion: The performance deficit of glaucoma patients which may be minimal under normal testing conditions is magnified when external noise is added to the stimulus. VEPs and psychophysical thresholds show interesting differences in their sensitivity to this effect. Implications for the early detection of glaucoma are discussed.

Key words: early detection, glaucoma, ideal observer, magneocellular pathway, noise, parallel pathways, parvocellular pathway, signal detection theory

Introduction

Primary open angle glaucoma is the second leading cause of blindness; in the industrialized world [1]. It is characterized by (1) increased intraocular pressure, (2) visual field losses, and/or (3) increased cupping of the optic disc. Visual field losses and increased disc cupping are presumed to result from ganglion cell death secondary to elevated intraocular pressure [2]. The

degenerated optic nerve fibers are distributed throughout the ON, indicating that ganglion cell damage is not limited to one area or type [3–5]. However, there does seem to be a greater loss of larger diameter ganglion cells [3–5]. Early treatment may be essential for preventing reversible loss of visual function; therefore, development of sensitive tests for early detection of primary open angle glaucoma would be a major step in blindness prevention [1].

Efforts at early primary open angle glaucoma (POAG) detection using visual fields and intraocular pressure have proven disappointing. A 5-db visual field deficit is required to demonstrate the presence of POAG. By the time visual field deficits of this magnitude may be detected about 20% of the optic nerve fibers in the affected region have degenerated [6]. Patients with increased intraocular pressure develop glaucoma at $\leq$ 1% per year [7]. Consequently, intraocular pressure while a major risk factor is not very predictive of who will develop glaucoma. Consideration of the underlying pathology might provide clues for creating sensitive glaucoma screening tests.

One way of conceptualizing the visual system is to think of it as consisting of a series of parallel pathways. One such set of pathways is the magnocellular (large cell) and parvocellular (small cell) pathways of the lateral geniculate nucleus. These two systems are segregated at the level of the retina and remain segregated at least until the visual cortex. More importantly they show distinctly different response properties. The magnocellular pathway is achromatic and responds physically to stimuli with lower spatial frequencies especially if they change rapidly. The parvocellular system has many color-opponent cells and responds tonically to stimuli which change slowly and/or have higher spatial frequencies [8–14].

Evidence suggests that glaucoma is marked by a loss of specific classes of retinal cells, large diameter retinal ganglion cells [3–6]. Some authors have interpreted this to suggest that glaucoma produces a loss in functions subserved by the magnocellular pathways (e.g., [15]). Early diagnosis would then best be accomplished by testing functions which are presumably mediated primarily by the magnocellular pathway such as flicker and motion detection [15–17]. However, there is also evidence of poor color vision in glaucoma patients [18]. Specifically, there is a marked deficit in the ability to detect blue objects on a yellow background [19]. Since color vision is a function mediated by the parvocellular system [9, 17], the effects of glaucoma cannot be assumed to be pathway specific (see [16, 17]).

An alternate hypothesis is that glaucoma affects a broad range of retinal cells, especially in its early stages [3–6]. Why then is it diagnosed by testing in the periphery and why are functions which depend on blue cones and large diameter ganglion cells often affected? It may be because these cell types are relatively few in number in the normal retina: (1) ganglion cell density is

lower in the periphery, (2) large diameter ganglion cells have lower density and (3) blue cone density is far lower than other cone classes. A general loss may affect these cells more, relatively speaking, because they are distributed more sparsely. This hypothesis has been referred to as the reduced redundancy hypothesis [16]. The functions of sparsely distributed cells may be more easily affected because of their smaller number under relatively standard testing conditions [16, 17].

Because of the potential benefits from early detection, there are many efforts to develop primary open angle glaucoma screening tests. These include measures of structure, e.g., optic nerve anatomy, retinal nerve fiber layer thickness, optic nerve blood flow, and measures of function, e.g., electrophysiological (pattern electroretinograms) [20] and behavioral tests (flicker sensitivity) [21]. Each of these strategies is recommended by a particular perspective or theory, either (1) of the underlying mechanism by which primary open angle glaucoma is generated or (2) of the effects of glaucoma on visual structures or functions. For example, the fact that ganglion cells die as a result of glaucoma underlies efforts at quantifying nerve fiber layer thickness. Similarly, suggestions that larger ganglion cells are more affected by glaucoma have led to the design of tests designed to test presumptive functions of these cells [15–17].

The inherent population variability of normal function presents severe problems for the development of successful tests of early glaucomatous damage. For example, the number of optic nerve fibers in normals has a standard deviation of about 20% of the mean [22, 23]. If the average number of optic nerve fibers and their standard deviation is initially the same in patients who do and do not develop glaucoma, then the number of fibers in an individual optic nerve must be reduced at least 40% before the nerve can be identified as abnormal with 95% confidence. Given the variability of the underlying anatomy, it seems unlikely that structural parameters will be considerably less variable than functional tests.

New approaches are needed to successfully screen for the early stages of glaucoma. Because the causes of early glaucomatous damage and the consequences of early damage remain uncertain, a new strategy should be general enough not to depend on any of the current assumptions about mechanisms of damage. One strategy is to develop tests that increase the mean difference between normals and primary open angle glaucoma suspects with early primary open angle glaucoma and/or reduce the groups' response variability. One may decrease the variability of normal subjects by using tasks to which they are very sensitive, for example, full field flicker [21]. Alternatively, one may increase the difference in group means. One means of increasing the differences between normals and patients with minimal defects should be

to increase the external noise. Therefore, visual tasks that artificially stress the visual system, increasing the demands placed on it, by adding external noise may be even more effective in identifying early neural damage from glaucoma (see the appendix for a derivation of the ideal observer model on which the strategy is based). The success of this strategy depends on the presumption that the visual system of the glaucoma patients is less efficient than that of normals [24–29]. However, the loss of cells in glaucoma requires that the system be less efficient.

There are several lines of evidence which support the utility of adding noise to stimuli. Simply presenting noise (snow) on a television screen has been shown to be a useful adjunct to perimetry. Patients experience scotomata which they otherwise fail to see subjectively [33]. Asking patients to detect a pattern as the correlation of its elements vary (i.e., noise is varied) [34, 35] can be useful in glaucoma detection. Most importantly, adding external noise has been used successfully to reveal functional visual loss in the elderly [30, 31] and in glaucoma patients [32].

Whether the same approach which appears to be successful with behavioral measures would also be successful with electrophysiological measures may be questioned. First, most electrophysiological measures make use of signal averaging which is a noise cancellation procedure. Nonetheless, several studies that used VEPs as a measure have suggested that VEPs elicited by stimuli which preferentially stimulate the magnocellular system may be useful in glaucoma detection [36, 37]. However, at least one study has argued that psychophysical measures and other measures may differ in their effectiveness for certain purposes [38] because they tap different levels of the visual system and reflect different internal noise sources [39]. In other words because they reflect different levels of visual processing, thresholds determined using VEPs and behavior might not behave the same way when noise is added to the stimuli. Another reason for being uncertain about the effects of noise is the question of what a threshold represents in the case of VEPs and behavior. In the case of behavior, we know that a threshold of a specific level corresponds to a d' of a certain level. There is no clear analogy in the case of VEP thresholds for stating that a VEP threshold represents a particular likelihood of identifying the stimulus correctly or that this corresponds to a particular d′ level.

In the present study we wished to compare contrast thresholds determined using stimuli thought to preferentially stimulate, either the parvocellular system (5.5 cpd) or the magnocellular system (7.5 Hz reversal of 0.69 cpd gratings). We wished to determine if adding noise improved the separation of the two normal and glaucoma groups as would be predicted by the theory.

Lastly, we wished to determine if adding noise to stimuli would affect contrast thresholds determined using VEPs or psychophysical methods differently.

Methods

Subjects

We tested 20 normal patients with a mean age of 39 years and 15 patients with early glaucoma with a mean age of 45 years. The six-year difference in mean ages was not statistically significant ($p > 0.1$). All patients had visual acuity of 20/20 or better at the viewing distance of 1 m. No patients had other visual diseases or systemic diseases that might have visual complications.

Stimuli and experimental procedures: Psychophysical estimates of contrast thresholds

Contrast thresholds were measured on two tasks: (1) 7.5 Hz reversing gratings of 0.69 cpd and (2) stationary 5.52 cpd gratings. Each task was tested at 5 noise levels ranging from 0 to 80% contrast. The screen size was 11.59 arc degrees at the viewing distance of one m. The mean screen illuminance was 68 lux. Noise was binary and was changed every 1/45th of a second (22.2 ms). Stimuli appeared for 666.67 ms (60 of 90 frames per second).

Thresholds were determined using a spatial four alternative forced choice method in conjunction with a staircase with a 1 up, 1 down rule, i.e., 50% correct ($d' = 0.84$). Prior to the beginning of each task, the subject was given an opportunity to practice the task. The choice of which task to present first was randomized. The sequence of testing within tasks was fixed. It began with the no added noise condition and progressed through the lower noise levels to the highest added noise condition.

Stimuli and experimental procedures: Sweep VEP estimates of contrast thresholds

The dependent measure in the sweep VEP experiments is an estimate of contrast threshold derived from the contrast sweep. It was calculated by extrapolating sweep VEP amplitude as a function of log contrast to zero voltage. In all of the sweeps, stimulus contrast decreased from high to low. The spatial frequency of the two stimuli was 5.5 cpd and 0.69 cpd. Noise was binary and changed every 1/30th of a second (33.3 ins). The stimulus frequency was 7.5 Hz. The stimuli appeared for 80 stimulus cycles or about 10.5 s. During each sweep, eight contrasts levels were presented for 10 stimulus

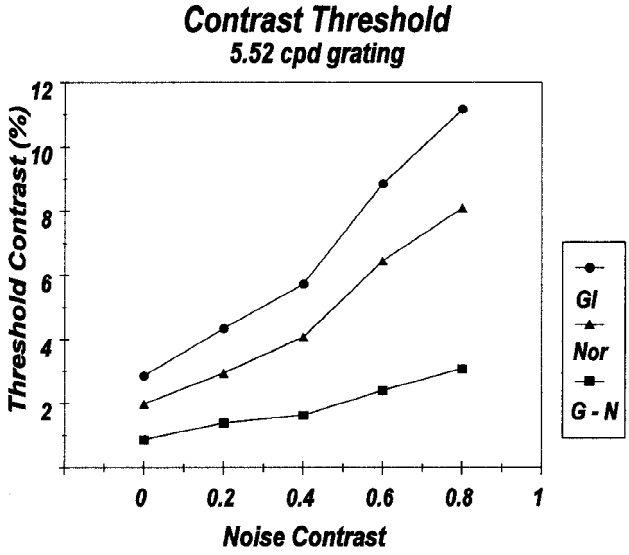

Figure 1. Psychophysical contrast thresholds of static 5.52 cpd grating as a function of noise contrast. Circles represent patients with early glaucoma, triangles represent normal subjects and squares represent the differences between the two groups. In the absence of added external noise there is not statistical significance between the groups ($p = 0.114$); a: 20% noise contrast the difference is statistically significant ($p = 0.046$) and becomes increasingly significant as noise contrast increases (at 40%, $p = 0.029$; at 60%, $p = 0.014$; at 80%, $p = (.00079)$.

cycles each, about 1.3 s per contrast step, for a total of 80 stimulus cycles and 10.5 seconds. The sweeps were repeated at three noise levels: 0%, 20% and 60% (rounded to nearest full percent).

Results

Psychophysical estimates of contrast thresholds

Differences in contrast thresholds were not statistically significantly different between the normal and patient groups at zero noise levels: Contrast thresholds of 5.52 cpd grating as a function of noise contrast ($p = 0.11$; see Figure 1), contrast thresholds of 0.69 cpd gratings reversing at 7.5 Hz ($p = 0.26$; see Figure 2).

The statistical significance of differences between normal and patients with early glaucoma in contrast thresholds of 5.52 cpd gratings increases as a function of noise contrast (see Figure 1); the difference is statistically significant at 20% noise contrast ($p = 0.046$) and becomes increasingly significant

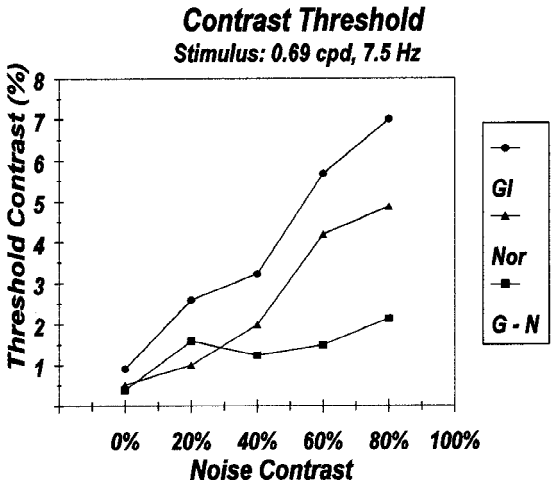

Figure 2. Psychophysical contrast thresholds of 0.69 cpd gratings reversing at 7.5 Hz as a function of noise contrast. Circles represent patients with early glaucoma, triangles represent normal subjects and squares represent the differences between the two groups. In the absence of added external noise there is not statistical significance between the groups ($p = 0.26$); at 20% noise contrast the difference is statistically significant ($p = 0.01$) and remains at approximately the same level as noise is increased (40%, $p = 0.026$; 60%, $p = 0.04$; and 80%, $p = 0.02$).

as noise contrast increases (at 40%, $p = 0.029$; at 60%, $p = 0.014$; at 80%, $p = 0.00079$).

The difference between glaucoma patients and normals for contrast thresholds of 0.69 cpd gratings reversing at 7.5 Hz remains relatively constant as noise is added; the level of statistical significance of the differences between the two groups is at 20%, $p = 0.01$; at 40%, $p = 0.026$; at 60%, $p = 0.04$; and at 80%, $p = 0.02$) (see Figure 2).

Sweep VEP estimates of contrast thresholds

The contrast thresholds determined using sweep VEPs were not statistically significantly different using 7.5 Hz reversal of 5.5 cpd gratings (see Figure 3). The 0.69 cpd gratings reversing at 7.5 Hz showed a statistically significant difference between the normal and glaucoma (see Figure 3). At the no noise level, the mean threshold percent contrast for the normal group was 0.382% $\pm$ 0.184 and for the glaucoma group was 1.014% $\pm$ 1.24 ($p = 0.029$). At the 20% noise contrast level, the mean threshold percent contrast for the normal group was 1.073% $\pm$ 2.911 and for the glaucoma group was 2.057% $\pm$ 4.597 ($p = 0.152$). At the 60% noise level, the mean threshold percent contrast for

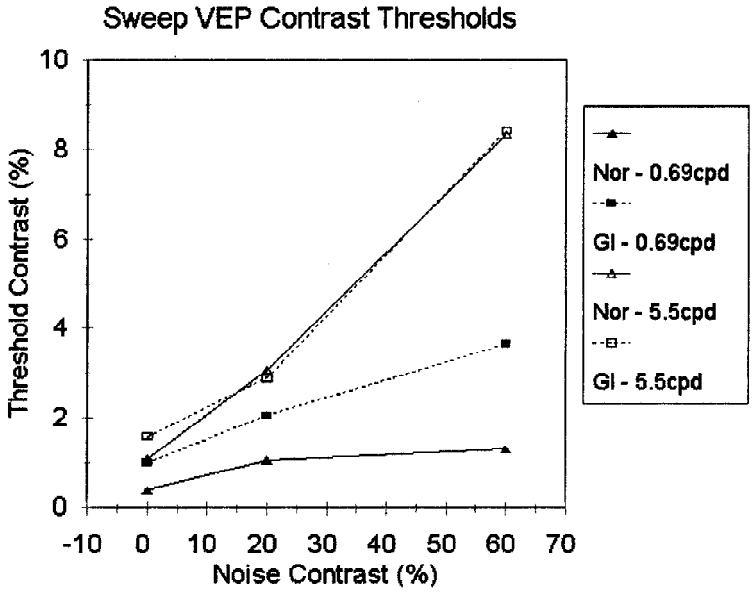

Figure 3. Sweep visually evoked potential contrast thresholds. The contrast thresholds determined using extrapolation of sweep VEP amplitude to zero voltage were not statistically significantly different at any noise level using 7.5 Hz reversal of 5.5 cpd gratings. The 0.69 cpd gratings reversing at 7.5 Hz showed a statistically significant difference between the normal and glaucoma (zero noise, $p = 0.029$; at 20% noise contrast level $p = 0.152$, and at 60% noise level $p = 0.03$).

the normal group was 1.305% $\pm$ 2.104 and for the glaucoma group was 3 660% $\pm$ 17.579 ($p = 0.03$).

Discussion

We described two major approaches to early detection of glaucoma. The first approach assumes that a specific class of retinal ganglion cells (and the related visual function) is more affected early in glaucoma. The second approach assumes that cells in general are affected even in early glaucoma. However, because some cells are more sparsely represented, some classes of cells (and related visual functions) will be more affected than others. In some ways both approaches are similar; both suggest that one should test for very specific visual functions. The difference between the approaches is in what one observes if one tests a variety of visual functions. The first approach suggests that some cells and their related functions will be unaffected by early glaucoma. The second strategy suggests that all cell classes and all functions will

be affected by early glaucoma, but that those functions subserved by more sparsely represented cells will be most affected. We noted that the inherent variability of underlying anatomy and physiology makes detecting defects in early glaucoma inherently difficult. Based on signal detection theory and ideal observers theory, we proposed a third approach. Namely we suggest that any visual function which is affected by early glaucoma will show a greater defect if external noise is added.

Under ordinary viewing conditions the difference between normal subjects and patients with early glaucoma may be minimal. As noise is added, we expected that performance would decline for both normals and patients. However, we expected that the change for patients would be greater, so that differences between the groups which were not significant when no external noise was present would be increased and become more statistically significant. We tested this general hypothesis using several different tasks. In general, our expectations were supported by our results.

Psychophysical estimates of contrast thresholds

Our data permit us to make several observations. (1) Without added noise, no statistically significant differences in contrast thresholds of gratings were present with the spatial frequencies tested. (2) When external noise was added, thresholds increased for normal subjects and patients with early glaucoma. Additionally, differences between the normal and glaucoma groups increased as noise increased both in absolute magnitude and statistical significance. This was particularly true of the 5.52 cpd, stationary grating. (3) The effects of adding noise saturated at relatively low noise contrasts when using a low spatial frequency, sinusoidally reversing grating. We discuss each of these results in more detail below.

Contrast sensitivity without external noise. Contrast sensitivity without added noise failed to discriminate between normals and patients with early glaucoma under any of the conditions that we examined. The performance deficits of patients with early glaucoma (or glaucoma suspects who have early glaucoma) are minimal when there is no added external noise. The conditions for testing contrast sensitivity without added noise were similar to standard conditions which might be used in a clinic. In other words, the conditions without added external noise would not be sensitive enough to detect differences between groups of normals and patients with early glaucoma.

External noise magnifies differences in contrast sensitivity. In general, the nonsignificant deficits which are present without added external noise are magnified when external noise is added to the stimulus. This is most clearly

seen in Figure 1 presenting data for the stationary 5.52 cpd gratings in which the differences and significance between groups increase as noise is added.

The effects of noise saturate at low contrasts for low spatial frequency stimuli. The data for the contrast thresholds of 0.69 cpd gratings reversing at 7.5 Hz presents an apparent exception to the conclusion that increasing noise contrast increases the difference between normal and glaucoma groups. While noise does increase the magnitude and significance of differences between the groups, the effect appears to saturate between a noise contrast of 20% and 40%. This particular stimulus was designed to stimulate the magnocellular system because of its low spatial frequency and relatively high temporal frequency. The response of magnocellular cells of the lateral geniculate nucleus saturate at about 30% contrast [8, 9]. This response saturation could impose a limit on the range of noise contrasts over which increasing noise contrast increasingly masks the stimulus. Drum and Bisset [35] reached a similar conclusion, observing that increasing noise contrast had little effect on coherency thresholds in a pattern discrimination task. It is possible that varying other parameters which alter noise energy (duration and spatial extent) may increase the effectiveness of masking for low spatial frequency, high temporal frequency stimuli.

Sweep VEP estimates of contrast thresholds

In the sweep VEP results, the effects of noise on thresholds were fundamentally different from those observed in the psychophysical studies and those predicted by theory. There was a significant difference between normals and patients with early glaucoma even in the absence of added noise. This significant difference was not magnified as external noise was added. The difference was not significant at 20%, but was significant at the same p level at 60% added noise as the no noise condition. Given our rate of stimulation, 7.5 Hz, we were probably preferentially stimulating the magnocellular pathway using these low spatial frequency stimuli. Therefore, the deficits revealed using the VEPs probably reflect magnocellular deficits in early glaucoma. This is consistent with previous reports that such stimuli are effective without added noise in separating normal and glaucomatous patients [35, 36]

The same pattern of results did not exist for the contrast thresholds of the 5.5 cpd gratings. At the no noise level there was no difference between the normal and early glaucoma groups. No difference emerged as external noise was added. There are two simplistic possibilities which could be used to account for these results. One may note that if no difference exists, multiplying it still yields a zero difference. This possibility is most interesting if we assume that we correctly tested the parvocellular system with the 5.5

cpd stimulus. The implication would be that there is little or no influence of glaucoma on the parvocellular system. We hesitate to draw this inference, however. First, at a temporal frequency of 7.5 Hz, we may be less effective in stimulating the parvocellular pathway. Therefore, failure to find differences between the groups using other stimuli may reflect inadequate stimulation of the parvocellular pathway. Second, we demonstrated a deficit using stationary 5.5 cpd gratings, psychophysically. A stationary 5.5 cpd grating probably more adequately stimulates the parvocellular system than the sweep VEP stimulus. Thirdly, others have demonstrated color vision deficits in glaucoma [18, 19] which are best interpreted in terms of a parvocellular effect [8–14].

In general, the effects of adding noise were minimal on the VEP contrast thresholds, at least in the ranges of noises available in the experiments. We can suggest at least three reasons for the difference between VEPs and psychophysics. First, most electrophysiological measures make use of signal averaging which is a noise cancellation procedure. Therefore, the effects of adding noise may be minimal. Second, psychophysical measures and electrophysiological measures may differ because they tap different levels of the visual system and reflect different internal noise sources [38, 39]. Third, thresholds calculated by extrapolation of VEP voltages do not represent the same differences between signal to noise as thresholds calculated from behavior. In the case of behavior, we know that a threshold of a specific level corresponds to a d' of a certain level. There is no clear analogy in the case of VEP thresholds for stating that a VEP threshold represents a particular likelihood of identifying the stimulus correctly or that this corresponds to a particular d' level. Moreover, it is not clear that thresholds calculated using extrapolation of VEP amplitudes would represent the same separation between signal and noise at the different noise levels tested.

Implications for strategies for early glaucoma detection

In the present study, we wished to determine if adding noise improved the separation of the two normal and glaucoma groups as would be predicted by theory. Also, we wished to determine if added noise might affect VEP and psychophysical contrast thresholds differently.

The present results are encouraging in that they show that our original framework for doing these studies is useful. Adding external noise does increase the separation between normals and patients with early glaucoma when psychophysical thresholds are measured. Our results confirm the observations that VEPs elicited by stimuli likely to stimulate the magnacellular pathway do discriminate between normal and glaucomatous patients. However, we failed to find evidence that adding external noise improved this separation. We have not demonstrated that the tests that we have employed could inde-

pendently be used to detect glaucoma. The results suggest that an optimized test battery of stimuli with added noise could improve screening accuracy and early detection of patients with glaucoma when measured psychophysically. Electrophysiological tests which might be a part of such a battery appear to function as well or better without added noise.

Appendix: Ideal Observer Theory/Signal Detection Theory applied to continuous representations of stimuli

In Signal Detection Theory, performance is limited by the signal-to-noise ratio [23–28].

$$d' = \sqrt{E_t/N} \tag{1}$$

where d'' is the sensitivity index, E_t is the signal energy at a given performance level and N is the spectral density of image noise.

Given this view and a statistical representation of an image, it is possible to construct a model, the Ideal Observer, which has no internal noise and uses all available signal information. Such an observer performs optimally in the sense that it is limited only by the information in the image.

Real observers, however, seldom achieve ideal performance. Previous authors have suggested three general factors to account for suboptimal human performance. The first is reduced information gathering efficiency. The Ideal Observer is a Bayesian classifier which determines p(hypothesis/data) for each potential signal. It computes a likelihood ratio for any two signals from the ratio of their probabilities. A decision rule uses the likelihood ratio or its monotonic transform to specify when the observer should say 'yes' or 'no'. The response transition point, the criterion, depends on what aspect of performance the observer wishes to optimize [24]. For most applications, this is assumed to be maximum percent correct.

The main problem, as in all Bayesian classification tasks, is to derive an estimate of p(data/hypothesis). The Ideal Observer obtains p(data/hypothesis) by cross-correlation of an optimal detector, a template exactly matching the expected signal, with the image. Performance would be decreased if the cross-correlation were compromised by using a suboptimal detector, by taking fewer samples, taking samples from too large or small an area, or by taking samples from the wrong location. The importance of proper sampling is apparent from Barlow's [23] definition of efficiency, F, as

$$F \frac{sample\ size\ required\ by\ the\ idea\ observer}{sample\ size\ required\ by\ the\ human\ observer} \tag{2}$$

F can be estimated directly from sensitivity as:

$$F = \frac{d'_e}{d'_i} \tag{3}$$

where d'_e is the experimentally obtained sensitivity and d'_i, is the sensitivity of an observer who uses all available information. Substituting (3) in (1) and rearranging produces the following relationship among detectability, threshold energy, noise and efficiency:

$$d'_e = \sqrt{f}\sqrt{E_t/N} \tag{4}$$

For an experimental performance level of $d' = 1$, the equation can be rewritten in terms of the energy threshold:

$$E_t = (1/F)(N) \tag{5}$$

The second factor producing suboptimal behavior is internal noise. The Ideal Observer is presumed to possess no internal noise. However, most detection devices also have internal noise which decreases detection performance. Internal noise may be represented by adding a term to Equation (5):

$$E_t = (1/F)(N_e + N_{eq}) \tag{6}$$

N_e refers to an external noise component and N_{eq} is a constant 'equivalent noise' [28] within the observer. (It is called 'equivalent' since it is internal noise which could be mimicked by an external noise of the equivalent level.)

One way to visualize the meaning of Equation (6) is to plot data from a hypothetical experiment which measures contrast energy needed to achieve a performance of d $d' = 1$ as a function of external noise spectral density. Figure 4 shows hypothetical results for such an experiment for an Ideal Observer (dotted line) who has an intercept of zero (is noiseless) and a slope of one (uses all information). Line A shows an observer with internal noise but optimum sampling efficiency. The internal noise adds a constant term producing a horizontal shift that can be quantified by the negative of the curve's intersection with the abscissa. Line B shows an observer with no internal noise but a lowered efficiency, which is quantified as the reciprocal of the slope. The division of visual factors into separate additive and multiplicative components, depicted in Figure 4 and Equation (6), has important implications for early detection and diagnosis of primary open angle glaucoma.

- The line's slope indicates the observer's sampling efficiency. If then were a loss of sampling elements, e.g., ganglion cells, or the same number of sampling elements were less sensitive then the slope would increase. Pathological conditions causing cell loss would be manifest as increased slope.

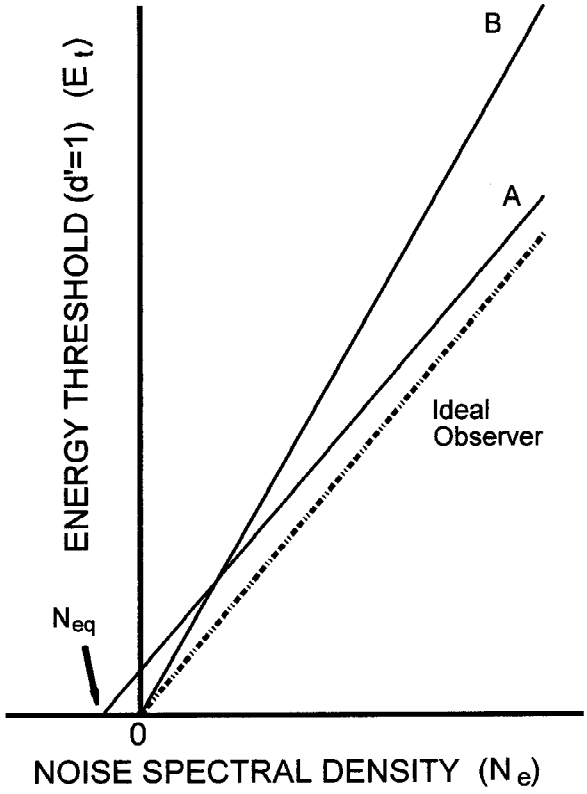

Figure 4. The results of hypothetical results of an experiment in which noise is added to stimuli and the energy threshold is measured. The results of three observers as shown. An ideal observer (dotted line) has an intercept of zero (is noiseless) and a slope of one (uses all information). Line A shows an observer with internal noise but optimum sampling efficiency (slope of one). Line B shows an observer with no internal noise but reduced efficiency (slope greater than one). The internal noise adds a constant term producing a horizontal shift that can be quantified by the negative of the curve's intersection with the abscissa. Loss of efficiency increases slope.

- The addition of external noise amplifies the visual loss. Small deficits, which may not be detectable in the absence of noise (i.e., using conventional displays at early stages of a disease), can become obvious in noise. In Figure 4, for example, the Ideal Observer and observer B are similar at low noise but different at high noise.

External noise should make it possible to detect primary open angle glaucoma earlier, when visual impairment is small and undetectable by normal methods.

- The dissociation of factors into additive and multiplicative components makes differential diagnosis more precise. At any one noise level, two observers could show identical sensitivity loss, yet one might suffer from

increased internal noise and the other from lower efficiency. The observers can be distinguished by testing at different external noise levels. For example, the effect of degraded optics, such as refractive error or reduced retinal illumination, is to add a constant internal noise which shifts the psychometric function without increasing slope (Observer A). Consequently, functional deficits due to optical factors would be distinguishable from deficits due to neural cell dysfunction or loss. Since most primary open angle glaucoma suspects are older, they may have optical losses and clinic personnel do not always correct refractions for test distances or for reduced retinal illumination.

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