process to a certain contrast is completed. If this steady-state response level falls in the middle of the corresponding contrast response function, one may conclude that the curve is actually centred to match the prevailing contrast level. This measurement was made before that of the corresponding contrast response function to ensure adaptation, and the results are shown as dashed lines in Fig. 1*a* and *b*. Note that these lines approximately go through the mid-points of the other contrast response functions (solid lines), establishing that the curves are, in fact, nearly centred to match the ambient contrasts.

The analogy we draw between the retinal sensitivity control mechanism for light intensity and contrast adaptation in the striate cortex is limited because all cortical cells do not show clear adapting behaviour of the type illustrated in Fig. 1*a* and *b*, while presumably, retinal neurones invariably adapt to prevailing light intensity levels. The adaptability of cortical cells to contrast varies from none to extensive. Figure 1*c* shows a complex cell which apparently did not adapt. All contrast response functions (solid lines) measured with different adapting contrasts and the steady-state response curve fall very close to each other, indicating fixed contrast–response properties for this unit. We found other cells, of both complex and simple types, which displayed no adaptation. One other type of unit that we recorded is of interest here. Of eight LGN afferents recorded in the striate cortex, none showed substantial adaptation. Figure 1*d* illustrates the results from an on-centre Y-cell from this group. As in the previous example (Fig. 1*c*), the contrast-response function of this LGN fibre was rigid, that is, it was not modified by adaptation. This suggests that contrast adaptation is primarily cortical in origin rather than occurring at the retinal or geniculate levels.

To facilitate comparisons, we computed an index of adaptability for each cell based on the slopes of the contrast–response functions. The index was computed by first normalizing the response and contrast ranges. By definition, the index is the mean of the slopes of the contrast response functions (solid lines in Fig. 1) minus the mean of the slopes of the curve connecting the mid-points of the functions at the adapting contrasts. For the cells we studied, the distributions of indices are unimodal and similar for simple and complex cells, with means and standard deviations of 0.52 ± 0.39 and 0.58 ± 0.41, respectively. Although this quantification is somewhat arbitrary, it suggests that contrast adaptation is a rule rather than an exception in the visual cortex, because most cells exhibit some degree of adjustment. On the other hand, indices for LGN fibres were very low (0.17 ± 0.22), reflecting their rigid contrast–response functions.

Considered together, these results have intrinsic functional significance, but they further suggest that caution must be used in trying to specify the absolute contrast threshold of cortical neurones. Our results demonstrate that the response amplitude and contrast threshold of a striate neurone can be strongly influenced by the contrast levels the cell has experienced in the recent past, even for contrasts as low as 6–10%. Previous investigations in which absolute contrast thresholds of cortical cells have been estimated have not included controls for the effects of adaptation when measuring contrast–response functions[6,7]. To illustrate this point, we used a procedure which was similar to that used in these other studies (all contrasts were presented in one randomized session) to generate a contrast–response function spanning the entire range. The result of this measurement is shown by dotted lines in Fig. 1*a* and *b*. Comparison of threshold estimates by extrapolation to the contrast axis shows clearly that these determinations tend to overestimate, or even possibly create, the contrast threshold, because of an overall adapting effect of the test stimuli.

We have shown that for most striate neurones, contrast adaptation behaves in a notably similar way to the retinal sensitivity control mechanism. Response–intensity curves in the retina and response–contrast curves in striate neurones shift laterally along log-intensity and log-contrast axes, respectively, so that they appropriately match prevailing input levels. We describe this mechanism in the cortex as contrast gain control, because of the lateral displacement of the central portion of the neurone's response curve along a logarithmic axis. This is equivalent to multiplicative or divisive scaling, although we cannot specify the exact underlying mechanism. Shapley and Victor have proposed a contrast gain control mechanism for cat retinal ganglion cells[8]. The mechanism we have investigated is probably quite different because we have found that LGN fibres show little contrast adaptation. Presumably, retinal neurones would behave similarly in this respect.

One may speculate on possible functions of contrast gain control in the cortex. For example, it may provide an advantage for the maintenance of a relatively high differential contrast sensitivity. Perhaps the visual system can cope with a wide range of contrasts because of this auto-ranging capability made available by contrast gain control. Alternatively, the outputs of neurones equipped with contrast gain control might provide inputs to possible succeeding pattern processors which must be capable of extracting pattern information regardless of the contrast of images. This can be realized by matching the input domain of pattern processors with that of image contrast through contrast gain control.

This work was supported by grant EY01175 and Research Career Development Award EY00092 from the US National Eye Institute to R.D.F. G.S. was supported by training grant EY07043.

Note added in proof: None of 27 cells recorded directly in the LGN showed significant adaptation.

Received 17 February; accepted 10 March 1982.

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Hyperacuity and amblyopia

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The most frequent cause of visual loss in childhood is functional amblyopia, an abnormality of visual acuity usually associated with either anisometropia (unequal refractive errors) or strabismus (turned eye) during early development. The usual clinical investigation of the visual acuity of amblyopes involves discrimination of the high contrast letters of a Snellen chart; however, there are other aspects of acuity, for example, grating acuity (the high spatial frequency limit of vision) and Vernier acuity (the smallest perceptible misalignment). Because of the extreme precision of Vernier acuity compared with either grating or Snellen acuity, it is considered to be a form of hyperacuity which requires very precise positional information. In an effort to understand the nature of the neural abnormalities which cause the reduced acuity of amblyopes, we have measured here the Vernier acuity of amblyopic observers using an extended Vernier grating stimulus, and compared these results with their Snellen acuity and grating acuity. The results showed that different acuity losses are associated with anisometropic versus strabismic amblyopia. When scaled with respect to their grating acuity, anisometropic amblyopes, like normals, showed hyperacuity, even at high spatial frequencies, while strabismic amblyopes showed severe losses in Vernier acuity. Snellen letter acuity showed a similar deficit relative to grating acuity in strabismic but not in anisometropic amblyopes. Contrary to some previous theories which have considered that all forms of amblyopia share a comon neural basis, these results strongly support the view[1,2] that different neural losses are associated with amblyopias of different aetiologies.

0028-0836/82/280268—03$01.00

The Vernier stimuli consisted of two rows of bright vertical lines on a dark background with an offset between the upper and lower rows; they are shown schematically in Fig. 1. The psychophysical paradigm was a self-paced method of constant stimuli. To obtain a criterion-free measure of the Vernier threshold a rating scale signal detection methodology was used[3]. Standard errors were generally 10–20% of the mean, and the per cent errors were similar in amblyopic and non-amblyopic eyes. Snellen acuity was determined using the E charts (depicted in Fig. 1) designed by Davidson and Eskridge[4] and grating acuity was measured using the same stimuli used to measure Vernier acuity. Figure 1 shows the relationship between Snellen acuity and low spatial frequency Vernier acuity (the fundamental spatial frequency of the Vernier gratings was at least 3 octaves below the resolution limit) for non-amblyopic eyes (open circles) and amblyopic eyes (lettered circles) for each observer. The non-amblyopic eyes, and most of the amblyopic eyes, showed Vernier acuities about four to five times better than Snellen acuity. The non-amblyopic eyes and the amblyopic eyes of the anisometropic amblyopes also showed low spatial frequency Vernier acuities which were about four times better than their grating acuity (Fig. 2). In contrast, the amblyopes with strabismus showed marked departures from this linear relationship.

If the amblyopic process affected Vernier acuity and grating acuity in the same way, it might be expected that Vernier acuity would be a constant percentage of the grating resolution limit. In the anisometropic amblyopes, Vernier acuity seems to be scaled in roughly the same manner as their grating resolution. This linear scaling of Vernier and grating acuities and also Vernier and Snellen acuities in anisometropic amblyopes, is evident in Figs 1 and 2, and the statistical analysis is shown in Table 1. These findings would be predicted if the aetiology of the visual loss was due to defocused retinal imagery early in life. The results of the amblyopes with strabismus showed Vernier acuities considerably worse than would be predicted from their grating resolution. In fact, two of the strabismics

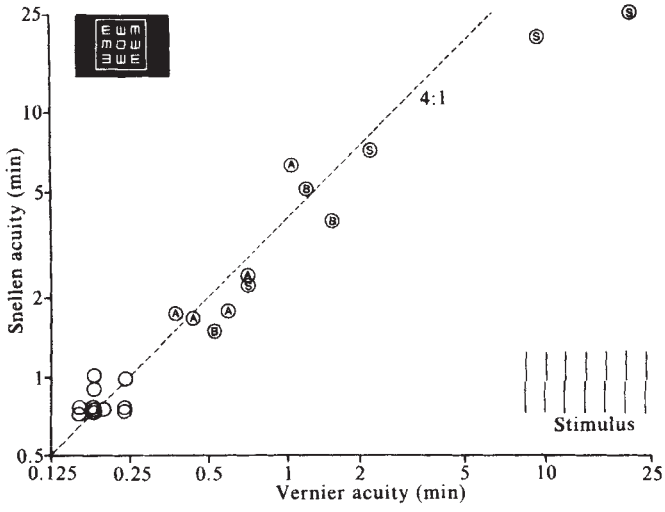

Fig. 1 Snellen acuity versus Vernier acuity (in min) for each eye of the 12 observers. The coordinates are log–log. Open circles are for non-amblyopic eyes. Circles containing A, S or B are for eyes with amblyopia due to anisometropia, strabismus and both strabismus and anisometropia, respectively. The Vernier acuity is for low spatial frequency gratings (at least 3 octaves below the resolution limit). The line represents a 4 : 1 relationship between Snellen acuity and Vernier acuity (that is, Snellen thresholds four times greater than Vernier thresholds). The inset on the upper left shows (in reverse contrast) the E charts used; the inset at the lower right shows the Vernier stimulus schematically. Note that the lines used were bright. Lines with random offsets were placed at the edge of the display to eliminate edge cues.

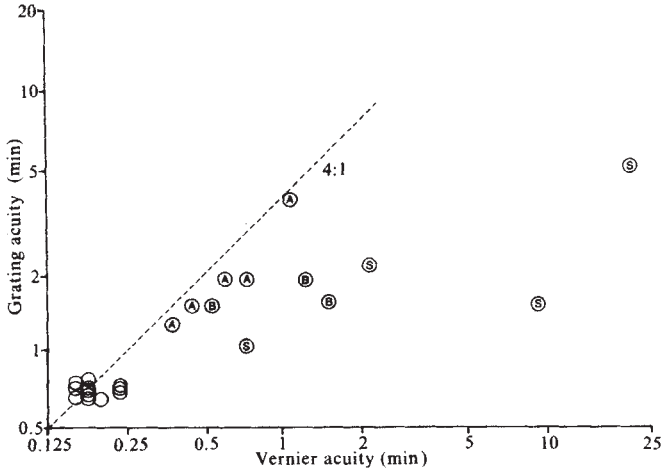

Fig. 2 Grating acuity (high spatial frequency cutoff) versus Vernier acuity (in min) for each eye of the 12 observers. Other details are as in Fig. 1. The grating acuity was determined via the method of adjustment, and the results shown are the mean of three ascending and three descending measures.

showed Vernier resolution which was two to three times poorer than their grating resolution (Fig. 2). Thus, in eyes with anisometropic amblyopia, Vernier acuity increases almost linearly with both Snellen and grating acuity (the exponents in Table 1 are close to 1.0 in anisometropic amblyopes). Snellen acuity also increases directly with grating acuity (exponent of 0.83). Strabismic amblyopes, on the other hand, show a specific loss of Vernier and Snellen acuity relative to grating resolution (the exponents relating both Vernier and grating acuity and Snellen and grating acuity are ~0.5). Interestingly, the relationship between the Vernier and Snellen acuities of these strabismic amblyopes more closely approximates linearity (exponent of 0.80). Thus, in strabismic amblyopia the grating acuity seems to be strongly decoupled from both Vernier and Snellen acuities. There is also evidence that cats with ablation of the striate cortex have only a mild loss of grating acuity, compared with a very dramatic loss of Vernier acuity[5]. Therefore, it may be that in strabismic amblyopia, striate cortical function (and therefore Vernier and Snellen acuity) is severely affected.

The results shown in Figs 1 and 2 were obtained at low spatial frequencies. In normal observers, Vernier thresholds are independent of spatial frequency over a wide range of spatial frequencies, increasing when the spatial frequency of the gratings is within about a factor of two of the observers' resolution (dotted line, Fig. 3). Similar results were obtained for anisometropic amblyopes (open symbols in Fig. 3); however, strabismic amblyopes (solid symbols, Fig. 3) showed a rather different result. For each of the amblyopes with strabismus, increasing the fundamental spatial frequency of the Vernier grating resulted in marked decreases in Vernier acuity from relatively high levels at spatial frequencies 4 octaves below the resolution limit, to a complete inability to perform the task for frequencies within 2 octaves of the resolution limit. In contrast, in all of the anisometropic amblyopes, Vernier thresholds remained constant up to 1 octave below the resolution limit. Thus, when scaled with respect to grating resolution, the anisometropic amblyopes are like normals in showing hyperacuity even at spatial frequencies approaching their grating resolution limit. Strabismic amblyopes, on the other hand, do not show hyperacuity at high spatial frequencies. This inability of strabismic amblyopes to maintain positional information at high spatial frequencies may be considered to be a form of 'crowding' phenomenon for Vernier discrimination[6]. Their comparable loss of acuity on the Snellen chart might be ascribed to the same deficit.

The present results cannot be explained on the basis of eccentric fixation, as the Vernier grating always included the

Table 1 Correlation coefficients and slopes of linear regression analysis of the relationships among Snellen, Vernier and grating acuity of each eye of amblyopic observers with anisometropia and strabismus

Subjects	n	Vernier versus Snellen		Vernier versus grating		Snellen versus grating	
		Correlation	Slope	Correlation	Slope	Correlation	Slope
Strabismic	14	0.98	0.80±0.04	0.91	0.42±0.05*	0.90	0.54±0.07*
Anisometropic	10	0.94	1.1 ±0.15†	0.96	0.94±0.09†	0.97	0.83±0.07

* Not compatible with a slope of 1 ($<10^{-10}$ chance that the data could be accounted for by a unity slope).
† Compatible with a slope of 1 (unity slope hypothesis cannot be rejected at the 5% significance level).

fovea in the stimulus field. Nor are the results readily explained on the basis of unsteady fixation, because rotating the display 90° so as to minimize the effects of horizontal fixation nystagmus, did not alter the results.

Several investigators have reported that strabismic amblyopes perceive distortions of space when viewing supra-threshold stimuli with the amblyopic eye[7–9]. If errors in spatial localization vary in time or across visual space, then tasks such as Vernier judgements at high spatial frequencies would be quite difficult. These spatial distortions seem to be primarily associated with strabismic amblyopia, perhaps resulting from abnormal binocular visual experience due to the strabismus. These results, in conjunction with the recent studies of Hess and Bradley[1], show that amblyopias resulting from different forms of visual deprivation have markedly different visual losses. While the results of Hess and Bradley suggest that anisometropic amblyopes are more handicapped in supra-threshold contrast processing, our results suggest that strabismic amblyopes are more handicapped in their ability to utilize positional information.

As Vernier acuity is such a high precision ability of the visual system, it may not be surprising that Vernier acuity should be severely compromised by the amblyopic dysfunction. What is surprising is that Vernier thresholds at high spatial frequencies are so different in amblyopias of different aetiologies.

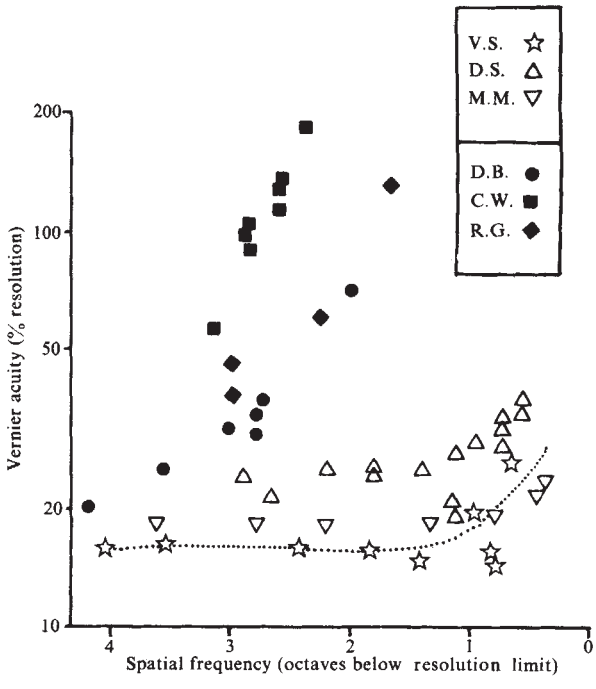

Fig. 3 Vernier acuity as a function of the fundamental spatial frequency of the grating. (The separation of the bright lines is the reciprocal of the fundamental spatial frequency of the grating.) Both the abscissa and the ordinate have been scaled to take into account each observer's grating resolution. The Vernier acuity (ordinate) is represented as a percentage of the grating resolution. The spatial frequency of the gratings (abscissa) is scaled in octaves (1 octave = 0.3 log unit) below the resolution limit. For non-amblyopic eyes, Vernier acuity is ~16% of the resolution limit for spatial frequencies an octave or more below the resolution limit (dotted line). Anisometropic amblyopes (open symbols) show similar results. The strabismic amblyopes (filled symbols) showed marked increases in Vernier acuity between 3 and 2 octaves below their resolution limit. The three strabismic and the three anisometropic amblyopes shown here have similar Snellen acuities.

We thank R. Harwerth, E. Smith and H. Bedell and R. Manny for helpful discussions. This research was supported by National Eye Institute grant RO1EY01728.

Received 18 January; accepted 17 May 1982.

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Sex difference in response to alphaxalone anaesthesia may be oestrogen dependent

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The steroid anaesthetic Althesin (Glaxo), which is a mixture of two C_{21} steroids, alphaxalone (3α-hydroxy-5α-pregnane-11, 20-dione—the active compound) and alphadolone acetate (21-acetoxy-3α-hydroxy-5α-pregnane-11, 20-dione), has been especially useful for the study of forebrain-autonomic[1] and neuroendocrine functions[2–5]. As determined by the loss of the righting reflex, Child *et al.*[6] found no sex difference in the anaesthetic dose of Althesin administered intravenously (i.v.). However, in our neuroendocrine studies[2–5] in which the anaesthetic was adminstered intraperitoneally (i.p.) and at dosage sufficient to produce surgical anaesthesia and analgesia, we observed a sex difference in the efficacy of Althesin. This may explain the difficulties that have been encountered in obtaining adequate anaesthesia (blockade of the somatomotor response to pain) with Althesin. Here we report, using cortical electroencephalography, that Althesin is a more potent anaesthetic than either sodium pentobarbitone or urethane, and that anaesthesia in the male rat requires about four times more Althesin (administered i.p.) than in the female. This sex difference is age dependent, can be abolished by administering oestrogen to the male, does not depend on sexual differentiation of the brain, and cannot be attributed to a sex difference in the metabolic clearance rate of alphaxalone. These results, taken together with those of Richards and Hesketh[7], suggest that the effect of alphaxalone may be mediated by interactions with synaptic membranes that are more specific than simply a generalized change in membrane structure, and that these interactions are affected by sex steroids.

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0028-0836/82/280270—03$01.00