Suprathreshold spatial frequency detection and binocular interaction in strabismic and anisometropic amblyopia

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We have investigated suprathreshold contrast sensitivity and binocular interactions in strabismic and anisometropic amblyopes using a reaction time paradigm. For every spatial frequency, reaction time increased as the grating contrast decreased. At all spatial frequencies and contrast values the reaction times using the amblyopic eye were prolonged compared to the nonamblyopic eye, but most markedly at high spatial frequencies. In the middle range of spatial frequencies, the contrast vs. reaction time function for the nonamblyopic eyes was biphasic, suggesting that two separate mechanisms detect gratings at high and low contrast levels. These functions in deep amblyopia were monotonic, and in shallow amblyopia the break in the functions was present but shifted to lower contrast levels. Binocular interaction experiments showed that binocular summation was absent at all contrast levels, but binocular occlusion was evident at high contrast levels for amblyopic observers.

Key words: amblyopia, binocular interactions, spatial frequency, contrast sensitivity, reaction-time, suprathreshold

It is well established that in the mammalian visual system there are at least two separate parallel channels termed X and Y, or sustained and transient channels, which differ in their physiological and morphological characteristics.1-10 Strabismus and anisometropia induced in kittens during the "critical period," results in reduced threshold contrast sensitivity and abnormal spatial resolution for high contrast gratings in the sustained neurons in the lateral geniculate nucleus.11-13 However, several studies have shown a selective loss of transient channels in cats raised with one eye occluded.14, 15

Several psychophysical strategies have been applied in order to differentiate the response properties of sustained and transient channels at threshold in the human visual system.16-19 These studies have suggested that channels which are thought to respond transiently to the onset and offset of stimuli operate mainly at low and moderate spatial frequencies and are particularly sensitive to flicker,17 rapid motion,18 and abrupt stimulus onset.19 Channels which respond in a sustained fashion for the total duration of the stimulus operate mainly at low and moderate and high spatial frequencies. The sustained channels are best stimulated by slowly moving or stationary stimuli.17, 18 These data indicate that sustained channels are responsible for the discrimination of spatial detail whereas the transient channels are responsible for detecting flicker and movement. Several psy-
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Table I. Visual characteristics of subjects

<table>
<thead>
<tr>
<th>Subject</th>
<th>Sex</th>
<th>Age</th>
<th>Visual acuity</th>
<th>Ametropia</th>
<th>Fixation</th>
<th>Binocular status</th>
<th>Previous treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>M. M.</td>
<td>M</td>
<td>29</td>
<td>RE 20/20</td>
<td>+0.75</td>
<td>Normal</td>
<td>6° E.T., L.E.</td>
<td>None</td>
</tr>
<tr>
<td>T. T.</td>
<td>F</td>
<td>23</td>
<td>LE 20/200</td>
<td>+2.00/−2.50 × 20</td>
<td>Unsteady, central</td>
<td>Normal</td>
<td>No strabismus</td>
</tr>
<tr>
<td>S. H.</td>
<td>M</td>
<td>15</td>
<td>RE 20/80</td>
<td>+6.50</td>
<td>Unsteady, central</td>
<td>Unsteady, central</td>
<td>6° E.T., R.E.</td>
</tr>
<tr>
<td>R. P.</td>
<td>M</td>
<td>34</td>
<td>RE 20/20</td>
<td>+5.00/−1.25 × 05</td>
<td>Unsteady, nasal</td>
<td>E.F., 1°</td>
<td>Direct occlusion at age 7</td>
</tr>
</tbody>
</table>

Recently, we have used a reaction time paradigm to study the detection of spatial frequency gratings at suprathreshold levels. The results showed that for a midrange of spatial frequencies, the reaction time vs. contrast plots were biphasic. This series of experiments on normal subjects indicated that for the particular stimulus parameters used, the sustained and transient channels operated over different contrast ranges. For spatial frequencies within this range, the transient channels were more efficient for high contrast stimuli, and the sustained channels were more sensitive at lower contrast levels. The present paper reports an application of this paradigm to the study of spatial vision and binocular interaction in amblyopia at suprathreshold levels.

Methods

Sinusoidal gratings were electronically generated on the cathode ray tube of an oscilloscope, and digital logic was used to control the experimental parameters and to time the stimulus durations and reaction time. A ready stimulus signaled the beginning of each trial, and when the subject depressed the response lever, a variable duration foreperiod was initiated. During this time the visual stimulus would occur with a 0.02 probability at the end of any consecutive 100 msec period. Reaction time was measured from the onset of the stimulus to the lever release by the subject. The gratings were on for a maximum of 500 msec. If the subject failed to release the lever within 1 sec following the stimulus onset, the trial was excluded from the data analysis. Thirty reaction time measures were made at each contrast level in blocks of 10 trials, in 0.1 log unit contrast intervals from threshold to a maximum of 44% or 75%. The standard error of the mean of the reaction times varied from approximately 4 to 8 msec at the short reaction times and 25 to 30 msec at the longer reaction times, being a constant 3% to 4% of the mean value, and did not significantly differ between the amblyopic and nonamblyopic eyes.

Subjects. The subjects were three strabismic and/or anisometropic amblyopes whose visual characteristics are shown in Table I. One observer (S. H.) had undergone previous direct occlusion treatment. Partial data was obtained on a fourth strabismic amblyope (R. P.). All subjects had clear ocular media and normal fundi and were appropriately corrected for refractive error during these studies.

Results

The relationship between reaction time and spatial frequency for gratings of the same physical contrast is shown in Fig. 1 for each of the three observers. The open circles are for the nonamblyopic eyes, closed circles are for the amblyopic eyes with a grating contrast of 0.75. As previously shown in normal ob-
servers,24–27 reaction time increases with increasing spatial frequency. The reaction times of the amblyopic eyes of each of the three subjects was considerably longer than that of the nonamblyopic eyes at higher spatial frequencies (greater than 4.0 cpd); however, at low spatial frequencies there appeared to be a "depth of anomaly" effect with M. M. showing the poorest acuity and the greatest increase in reaction times and with S. H. showing the best acuity and the smallest difference in reaction times. We have noted a similar depth of anomaly effect at threshold.28 The diamonds in Fig. 1, B, show the phase lag of the steady-state visual evoked potential (VEP) to the onset/offset of spatial frequency gratings for Subject T. T. Although the evoked potentials were obtained with a larger screen with a P 31 phosphor and a contrast of 0.44,29 there was considerable similarity in the VEP and reaction time data. Fig. 1, C, (Subject M. M.) also shows reaction time vs. spatial frequency data for gratings with a contrast of 0.375 and 0.075 for the nonamblyopic eyes (open symbols) and amblyopic eyes (closed symbols). It is clear from these data that the difference between the two eyes was greater with gratings of lower contrast than with high contrast gratings.

Fig. 2 illustrates the relationship between reaction time and contrast for six spatial frequencies for both eyes of amblyopic Observer M. M. An inverse covariation between reaction time and contrast was seen for all spatial frequencies. For the nonamblyopic eye (open circles), the data for spatial frequencies greater than 0.50 cpd show a discontinuity in the lower part of the function, suggesting that under these conditions, two separate mechanisms determine the reaction time, one operating at low contrast levels, the other at high contrast levels. Previous experiments24 in which field size, retinal location, and viewing duration were varied suggest that the biphasic function occurs as a result of the sustained and transient channels operating over different contrast ranges. Within a midrange of spatial frequencies the transient channels, which have a shorter response latency than the sustained channels, are more sensitive to the stimulus parameters used in these experiments at high contrast levels; however, at lower contrast levels, the sustained channels become more effective, and at the detection threshold, they are the
Fig. 2. Mean reaction time as a function of contrast for the spatial frequencies indicated (Subject M. M.). Open circles show data for the nonamblyopic eye; solid circles, data for the amblyopic eye. The curves shown are templates (see text for details of curve fitting).

more sensitive channels. The data of the nonamblyopic eye of Observer M. M. have been fit with two template curves, in a manner similar to that described by Stiles for pi mechanisms. The data above 0.50 cpd for the nonamblyopic eyes required both templates to adequately describe both the high and low contrast portions of the curves; however, the 0.50 cpd data were adequately fit by the high contrast (transient) template. It is interesting to note that none of the curves for the amblyopic eye showed a break. These data were adequately fit by simply shifting the high contrast (transient) template of the nonamblyopic eye up. For all spatial frequencies, even at high contrast levels, the reaction times were longer for the amblyopic eye than the nonamblyopic eye, and the difference between the two eyes increased with higher spatial frequencies. Tolhurst has shown that the frequency distribution of reaction times for transient channels is bimodal, since they respond both at the onset and offset of the stimulus, whereas that of sustained channels is unimodal for near threshold stimuli. Fig. 3 shows reaction time frequency distributions for the nonamblyopic and amblyopic eyes of Subject M. M. for gratings of 0.50 and 4.0 cpd for near threshold contrast. For the 0.50 cpd gratings both eyes showed a clearly bimodal distribution, thus confirming Tolhurst’s findings at low spatial frequencies. At 4.0 cpd the frequency distribution of reaction times for the nonamblyopic eye was unimodal, suggesting that at threshold, detection is via sustained channels. However, the amblyopic eye showed a bimodal distribution of reaction times for spatial frequencies as high as 4.0 cpd. Thus the detection of spatial contrast at threshold...
Fig. 3. Reaction time histograms for the spatial frequencies indicated for Subject M. M. A and C, Nonamblyopic eye. B and D, Amblyopic eyes. The bin width was 50 msec.

Fig. 4. Isocontrast functions derived from the reaction-time data shown in Fig. 2 for the nonamblyopic eye, A, and the amblyopic eye, B, of Subject M. M. The number at the end of each curve shows the criterion reaction time used to obtain the function. The mean luminance was 10 cd/m² and maximum contrast was .44.
may be mediated by transient channels at higher spatial frequencies in the amblyopic eye than in the nonamblyopic eye.

Functions which relate the stimulus contrast that produces equal perceptual effects across spatial frequencies may be derived by plotting the contrast value for a criterion reaction time at each spatial frequency. These suprathreshold "isocontrast" functions are shown for the nonamblyopic and amblyopic eyes of M. M. in Figs. 4, A and B, respectively. The number at the end of each curve shows the criterion reaction time used to derive the function. The data for the nonamblyopic eye were similar to those of normal subjects. The top curve is the threshold function. The lowest curve (260 msec criterion reaction time) should be a pure transient channel contrast sensitivity function, with the higher curves representing a mixture of sustained and transient channel sensitivity and the curves determined by reaction time of 380 msec or longer primarily representing sustained channel activity.

For the amblyopic eye, the sensitivity for each criterion reaction time was lower, and the function showed a peak shift to the lower spatial frequencies and a narrower shape for the long reaction times with less marked low frequency attenuation. The difference between the shapes of the curves for two eyes was less marked for the short reaction times. For example the lower three curves for the amblyopic eye were similar in shape to the lower three curves for the nonamblyopic eye, although in each case the amblyopic eye curves were derived by a longer criterion reaction time. Comparing the whole series of isocontrast functions shows that the systematic shift from the transient to the sustained channels seen in the data of the nonamblyopic eye did not occur in the amblyopic eye.
Fig. 6. Isocontrast functions for the nonamblyopic eyes (left column) and amblyopic eyes (right column) of Subjects M. M., T. T. and S. H. The number at the end of each curve shows the criterion reaction time used to obtain the function. The mean luminance was 76 cd/m², and the maximum contrast 0.75.

These studies were conducted with a maximum contrast of 44% and a mean luminance of 10 cd/m². We repeated these experiments on Subject M. M. with a higher mean luminance (76 cd/m²) and a maximum contrast of 75%, with similar results. Fig. 5 shows the reaction time vs. contrast data obtained under these conditions for the nonamblyopic and amblyopic eyes of each of the subjects for gratings of 4.0 cpd. Although there were individual differences in the positions and strength of the breaks in the function of the nonamblyopic eyes, only Subject S. H. (the subject with the best visual acuity) showed a break in the data of the amblyopic eye, requiring the use of both templates for an adequate fit to the data. Interestingly, the break in the curve of the amblyopic eye was shifted to the left (i.e., toward lower contrast levels than the nonamblyopic eye). Suprathreshold isocontrast functions for M. M., T. T., and S. H. obtained under the higher luminance and contrast conditions are shown in Fig. 6.

The data obtained at this higher luminance were similar to those for Subject M. M. (Fig. 4); the curves for the amblyopic eye showed lower threshold and suprathreshold contrast sensitivity for all criterion reaction times, and the peak shift to the left at threshold was still evident at this higher luminance level. The curves for the two eyes of Subject S. H. showed little difference at low spatial fre-
Binocular interactions at and above threshold. In order to evaluate binocular interactions at and above threshold, we have plotted the ratio of binocular to monocular contrast required for different criterion reaction times. The data in Fig. 7, A, B, and C, show the contrast required under binocular viewing for a given criterion reaction time plotted against the contrast required by the nonamblyopic eye to give the same criterion reaction time. The data are for three amblyopic observers, and in the case of the two strabismic amblyopes (M. M. and R. P.), prisms were applied to ensure bifoveal fixation. (Both M. M. and T. T. have normal retinal correspondence, whereas R. P. has anomalous retinal correspondence). The solid line shows a ratio of 1 (i.e., the sensitivity under binocular viewing is equal to that of the nonamblyopic eye); the dashed line shows binocular summation, and points below the solid line show occlusion (i.e., the binocular is less than that of the nonamblyopic eye on its own). The data for these observers were interesting in that they all showed a ratio equal to approximately 1 at near threshold values. Subjects M. M. and T. T. showed occlusion at higher contrast levels whereas Observer R. P. showed a ratio of 1 at all levels. This is of particular interest since normal observers generally show at least partial binocular summation at higher contrast levels and binocular contrast sensitivity is greater than monocular sensitivity by approximately $\sqrt{2}$ at threshold.

The monocular testing reported to this point was conducted with the untested eye patched with a black occluder. In order to further evaluate binocular interactions, we determined reaction time as a function of grating contrast, with the untested eye viewing through a diffuser, so that the input to the untested eye was a structureless field of the same average luminance as the test field. For Subjects R. P. and T. T., the monocular data were uninfluenced by the input to the untested eye; however, the data of M. M. (Fig. 8) are rather interesting. The solid symbols show the data for the nonamblyopic eye (circles) and amblyopic eye (triangles) with the untested eye patched; open symbols are the data with the untested eye viewing through a diffuser. The squares show the data for binocular viewing. The data of the nonamblyopic eye showed longer reaction times for

![Fig. 7. Ratio of the contrast required under binocular viewing is plotted against that required when the nonamblyopic eye views for the criterion reaction times shown. The solid line shows a ratio of 1, i.e., the binocular contrast sensitivity is equal to that of the nonamblyopic eye. The dashed line shows perfect summation and the shaded area partial summation. Points falling below the solid line show occlusion (i.e., binocular sensitivity lower than that of the nonamblyopic eye).](http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933085/)
Fig. 8. Reaction time vs. contrast for 4.0 cpd gratings for Subject M. M.

the higher contrast levels when the amblyopic eye viewed through a diffuser. Over the entire contrast range, the binocular to monocular ratio was equal to approximately 1 when the amblyopic eye viewed through the diffuser. Thus, at higher contrast levels, it appeared that the amblyopic eye may inhibit the sensitivity of the nonamblyopic eye. Similarly, the amblyopic eye was suppressed in sensitivity when the nonamblyopic eye viewed through a diffuser; however, this suppression of the amblyopic eye was most marked at low contrast levels (up to approximately 1 log unit above threshold). It is not clear why the binocular interactions differ in these observers; however, Subject M. M. occasionally experiences diplopia on removal of his spectacle correction.

Discussion

The results of these experiments are in agreement with those of previous studies which have shown increased reaction time to spots of light. \(^{37, 38}\) The data presented in this report extend these findings to the contrast domain and show that reaction time is prolonged in amblyopic eyes for a wide range of spatial frequencies and over a range of contrast values extending from threshold to several log units above threshold; the increased reaction time is most pronounced at higher spatial frequencies. These findings are in agreement with the increased phase lag in the visual evoked response of the amblyopic eye to grating patterns\(^ {29}\) (cf. Fig. 1, B), and further support the contention that there is no suprathreshold compensation for the reduced contrast sensitivity in strabismic and anisometropic amblyopes as has been shown in some meridional amblyopes.\(^ {39}\)

These reaction time studies provide new information in confirming the biphasic nature of the reaction time vs. contrast functions in the middle spatial frequency range in normal eyes\(^ {24}\); however the data for the amblyopic eyes appear to be monotonic in deep amblyopes and show a shift in the break in Subject S. H. who shows shallow amblyopia. The results of our previous investigations on normal observers\(^ {24}\) suggest that the biphasic function reflects the activity of two mechanisms with different contrast operating ranges. For spa-
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Toral frequencies between 1 and 8 cpd the transient channels are more efficient for high contrast stimuli, and sustained channels are more sensitive at lower contrast levels. Tolhurst has shown that the distribution of reaction times for transient channel activity is unimodal. In the amblyopic eye, even at spatial frequencies as high as 4.0 cpd, the distribution is bimodal (cf. Fig. 3). Thus the detection of spatial contrast in amblyopic eyes may be mediated by transient channels at higher spatial frequencies than the non-amblyopic eye. However, the transient channels are probably also somewhat affected at least in deeper amblyopes, since even high contrast stimuli of all spatial frequencies resulted in prolonged reaction times, as did the 1° spot used by von Noorden. This is also seen in the perceptual isocontrast functions (Figs. 4 and 6). These data show the contrast sensitivity of the amblyopic eye to be reduced at threshold across a wide range of spatial frequencies. At each criterion reaction time, the suprathreshold contrast sensitivity of the amblyopic eye is also reduced; although, at the shorter criterion reaction times, the curves are more similar for the two eyes. The present study also suggests that there may be a depth of anomaly effect, with the deeper amblyopes showing more low spatial frequency loss than the shallower amblyopes and the shallower amblyope retaining the biphasic contrast vs. reaction time function at 4.0 cpd. The reaction time data reported here suggest that both the sustained and transient channels may be affected in patients with strabismic and anisometric amblyopia but that the sustained cells are more severely affected. It appears that the effect of strabismus and anisometropia on the developing nervous system is greatest for high spatial frequencies. Presumably neurons with small receptive fields are most affected, whereas neurons with large receptive fields are less affected. Since sustained neurons have small receptive fields, the anomaly must be primarily in the sustained channels. Ikeda and Wright have proposed that amblyopia may result when the foveal sustained neurons do not receive adequate stimulation during a sensitive period of development and that a functional degeneration of the sustained cells could occur as early as the retinal ganglion cells. Such an anomaly may be independent of the loss of binocularity seen in kittens reared with experimentally induced esotropia or exotropia.

We have used the reaction time paradigm to investigate binocular interactions in amblyopia at and above threshold. The data reported (Fig. 7) suggest that at near-threshold values the amblyopic eye is totally suppressed, and not even probability summation is evident in the binocular data. For Observer R. P., the binocular sensitivity was identical to that of the nonamblyopic eye at any criterion reaction time. For the other two observers, at higher contrast levels, occlusion occurred, with binocular sensitivity being lower than that of the nonamblyopic eye alone. Abnormal binocular interactions of this type in amblyopes have recently been reported in the evoked potential to high contrast gratings. In addition, the data of Subject M. M. show that when the untested nonamblyopic eye is presented with a homogeneous field of the same average luminance, there is a suppression of the sensitivity of the amblyopic eye particularly at low contrast levels. Suppression of the amblyopic eye by the nonamblyopic eye has been previously shown to occur for letters, and von Noorden has shown that reaction time to a 1° spot of light is most prolonged in the amblyopic eye, at threshold levels under binocular viewing. Interestingly, the amblyopic eye also appears to exert a suppressive effect on the nonamblyopic eye at high contrast levels (Fig. 8). Similar findings have been reported in the evoked potentials of strabismic amblyopes.

Since most of the stimuli to which the visual system responds are well above threshold, the present data provide a needed characterization of the monocular and binocular performance characteristics of amblyopic eyes at suprathreshold levels and further suggest that the primary anomaly in strabis-
mic and anisometropic amblyopia involves the sustained channels, with transient channels being less affected.

REFERENCES