Increased Binocular Enhancement of Contrast Sensitivity and Reduced Stereoacuity in Duane Syndrome

Wendy E. Marshman,1 Emma Dawson,1 Majella M. Neveu,1 Michael J. Morgan,2 and John J. Sloper1

PURPOSE. To compare the binocular enhancement of contrast sensitivity and stereoacuity in patients with Duane syndrome and normal subjects.

METHODS. Monocular and binocular contrast sensitivity functions were determined using a two-alternative, forced-choice method in 14 patients with Duane syndrome and 14 normal subjects. Monocular and binocular log minimum angle of resolution (logMAR) acuities were measured, and stereoacuity was determined using the Titmus and TNO stereotests.

RESULTS. In the patients with Duane syndrome, the binocular enhancement of contrast sensitivity was increased across all spatial frequencies, although stereoacuity was reduced compared to that of the normal subjects. The increased enhancement was caused by a reduction in monocular contrast sensitivity rather than an increase in binocular contrast sensitivity. The patients with Duane syndrome also showed a generalized reduction of contrast sensitivity at high spatial frequencies.

CONCLUSIONS. It is suggested that the combination of reduced stereoacuity and increased binocular enhancement of contrast sensitivity seen in Duane syndrome can be explained by a partial loss of binocular cortical cells, caused by intermittent misalignment of the eyes during early visual development.


Patients with Duane retraction syndrome typically have reduced abduction of one eye, with retraction of the globe on attempted adduction.1–3 This is thought to be due to a primary abnormality of the sixth cranial nerve, with aberrant innervation of the lateral rectus muscle by fibers from the third nerve.4 In a recent study, magnetic resonance imaging (MRI) showed the absence of the VI nerve nucleus.5 Most patients with Duane syndrome are able to maintain binocular single vision by using an abnormal head posture, but they have an intermittent manifest squint. This is present during the sensitive period of visual development. Although such patients have binocular single vision, they have mildly reduced stereoacuity when compared to normal subjects,6,7 and a variable degree of suppression is found during misalignment.7–9 This raises the question of whether there are other abnormalities of binocular function in these patients, which may give further information about the effects of intermittent motor misalignment on sensory visual development.

One aspect of binocular interaction is binocular summation, which is said to occur when detection is performed better with two eyes than with one. For example, Campbell and Green10 measured contrast sensitivity for sinusoidal gratings of different spatial frequencies and found that binocular sensitivity was approximately 1.4 (√2) times better than monocular sensitivity. This is the value for binocular enhancement that is predicted by simple summation of two independent noisy signals. For a recent review of other experiments and theoretical considerations, see Howard and Rogers.11 The present study has extended the investigation of binocular function in patients with Duane syndrome by measuring binocular and monocular contrast sensitivity functions and comparing the degree of binocular enhancement to that in a control group of normal subjects.

These data have been presented previously in abstract form.12

SUBJECTS AND METHODS

Fourteen patients with Duane retraction syndrome were studied, together with fourteen normal subjects of a similar age range (Tables 1 and 2). Patients were approached either during a clinic visit or were contacted from clinic records and were the first 14 patients with Duane syndrome and binocular single vision who were willing to participate in the research. All patients underwent orthoptic assessment of ocular motility, together with measurement of monocular and binocular logMAR visual acuities and TNO and Titmus stereoacuity tests, while wearing appropriate spectacle correction if required. Each patient was given time to adopt the optimum head posture for stereoacuity measurements.

Monocular and binocular contrast sensitivity functions were measured by a spatial two-alternative, forced choice (2AFC) procedure on computer (using Psycho for Windows ver. 2.29 software; Cambridge Research Systems [CRS], controlling a CRS VSG 2/4 graphics board and high-resolution monitor). The stimulus was a 10.4° diameter circular grating with vertical sinusoidal contrast modulation presented at 1-m viewing distance. Stimuli were presented for 5.5 seconds with a 0.5-second attack and 0.5-second decay, and the center was slightly offset to the right or left of the screen center. Subjects had to indicate which side the target appeared. Mean stimulus luminance was 64.9 candelas (cd)/m². Contrast sensitivity was measured at six spatial frequencies; 0.5, 1.0, 2.0, 4.0, 8.9, and 17.8 cyc/deg. The linear staircase had a decrease of 1.0 dB for one right answer and an increase of 3.0 dB for one wrong answer. Threshold was calculated as the mean contrast over the last 10 reversals.

Left eye, right eye, and binocular functions were recorded in random order. Monocular contrast sensitivities were recorded with the other eye occluded by a +10-diopter (D) sphere Fresnel lens. At each
spatial frequency, binocular enhancement was measured both as the binocular contrast sensitivity divided by the mean of the two monocular contrast sensitivities and as the binocular contrast sensitivity divided by the best monocular contrast sensitivity. Contrast sensitivity at the highest spatial frequency was not measured in four patients and five normal subjects, and data for this spatial frequency have therefore been excluded from the analysis of variance.

Statistical comparisons between results for left and right, or affected and fellow, eyes were made with a paired \( t \)-test and between the patients and normal subjects, with an unpaired \( t \)-test. Differences in stereoacuity were analyzed using the Mann-Whitney test corrected for tied values. Contrast sensitivity data were analyzed using analysis of variance (ANOVA). Because Duane syndrome most commonly affects left eyes, the affected eyes of the patients were compared to left eyes in normal subjects and the fellow eyes to normal subjects’ right eyes.5,7,13

The research conformed with the tenets of the Declaration of Helsinki. The subjects gave informed consent after explanation of the nature and possible consequences of the study. The research was approved by the Ethics Committee of Moorfields Eye Hospital.

## Results

Nine patients had unilateral Duane syndrome, of whom seven had affected left eyes and two had affected right eyes (Table 1). Five patients were bilaterally affected, three being more affected in the left eye and two in the right. All patients showed typical limitation of abduction of the affected eye with retraction on attempted addition. All maintained bifoveal binocular single vision by using an abnormal head posture.

### Visual Acuity

Monocular and binocular logMAR visual acuities for the patients with Duane syndrome are shown in Table 1 and for the control group in Table 2. The small difference between affected and fellow eyes of the patients did not reach significance \((t = 1.99; P = 0.067; df = 13)\). However, the affected eyes of the patients were slightly worse than the left eyes of the control group \((t = 2.42; P = 0.023; df = 26)\); there was no significant difference between the fellow eyes of the patients and the right eyes of the control group \((t = 1.39; P = 0.17; df = 26)\). Both patients and normal subjects showed significant binocular enhancement of acuity, binocular acuity being better than mean monocular acuity (Duane group, \(t = 2.85, P = 0.017, df = 13\); normal group, \(t = 2.77, P = 0.016, df = 13\)). There was no difference between the two groups in the degree of binocular enhancement of acuity \((t = 0.34, P = 0.73, df = 26)\).

### Table 1. LogMAR Acuities and Stereoacuities of 14 Patients with Duane Syndrome

<table>
<thead>
<tr>
<th>Subject</th>
<th>Affected Eye</th>
<th>Age (y)</th>
<th>Fellow Eye</th>
<th>Affected Eye</th>
<th>Binocular TNO (Seconds of Arc)</th>
<th>Titmus</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Left</td>
<td>9</td>
<td>0</td>
<td>0.2</td>
<td>0</td>
<td>60</td>
</tr>
<tr>
<td>2</td>
<td>Right &gt; left</td>
<td>16</td>
<td>-0.1</td>
<td>0.1</td>
<td>-0.1</td>
<td>120</td>
</tr>
<tr>
<td>3</td>
<td>Left</td>
<td>8</td>
<td>0.1</td>
<td>0.3</td>
<td>0.1</td>
<td>60</td>
</tr>
<tr>
<td>4</td>
<td>Right</td>
<td>10</td>
<td>-0.04</td>
<td>0.02</td>
<td>0.02</td>
<td>60</td>
</tr>
<tr>
<td>5</td>
<td>Right</td>
<td>12</td>
<td>-0.1</td>
<td>0</td>
<td>-0.1</td>
<td>60</td>
</tr>
<tr>
<td>6</td>
<td>Left &gt; right</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>60</td>
</tr>
<tr>
<td>7</td>
<td>Right &gt; left</td>
<td>17</td>
<td>-0.18</td>
<td>-0.18</td>
<td>-0.18</td>
<td>60</td>
</tr>
<tr>
<td>8</td>
<td>Left</td>
<td>15</td>
<td>-0.02</td>
<td>0</td>
<td>0</td>
<td>60</td>
</tr>
<tr>
<td>9</td>
<td>Left &gt; right</td>
<td>14</td>
<td>-0.1</td>
<td>-0.08</td>
<td>-0.08</td>
<td>60</td>
</tr>
<tr>
<td>10</td>
<td>Left &gt; right</td>
<td>8</td>
<td>0.1</td>
<td>-0.1</td>
<td>-0.1</td>
<td>60</td>
</tr>
<tr>
<td>11</td>
<td>Left</td>
<td>47</td>
<td>0</td>
<td>0.1</td>
<td>0</td>
<td>120</td>
</tr>
<tr>
<td>12</td>
<td>Left</td>
<td>14</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>120</td>
</tr>
<tr>
<td>13</td>
<td>Left</td>
<td>37</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>120</td>
</tr>
<tr>
<td>14</td>
<td>Left</td>
<td>24</td>
<td>-0.1</td>
<td>0</td>
<td>-0.16</td>
<td>60</td>
</tr>
<tr>
<td>Mean</td>
<td>17.1</td>
<td>-0.02</td>
<td>0.03</td>
<td>-0.04</td>
<td></td>
<td>75</td>
</tr>
</tbody>
</table>

### Table 2. LogMAR Visual Acuities and Stereoacuities of 14 Normal Subjects

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (y)</th>
<th>Right Eye</th>
<th>Left Eye</th>
<th>Binocular TNO (Seconds of Arc)</th>
<th>Titmus</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>35</td>
<td>-0.1</td>
<td>-0.1</td>
<td>-0.1</td>
<td>30</td>
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<tr>
<td>16</td>
<td>39</td>
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<td>-0.3</td>
<td>-0.3</td>
<td>15</td>
</tr>
<tr>
<td>17</td>
<td>12</td>
<td>-0.2</td>
<td>-0.1</td>
<td>-0.2</td>
<td>30</td>
</tr>
<tr>
<td>18</td>
<td>11</td>
<td>0</td>
<td>-0.1</td>
<td>-0.1</td>
<td>30</td>
</tr>
<tr>
<td>19</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>60</td>
</tr>
<tr>
<td>20</td>
<td>9</td>
<td>-0.1</td>
<td>0</td>
<td>-0.1</td>
<td>30</td>
</tr>
<tr>
<td>21</td>
<td>13</td>
<td>-0.4</td>
<td>-0.2</td>
<td>-0.24</td>
<td>60</td>
</tr>
<tr>
<td>22</td>
<td>13</td>
<td>-0.1</td>
<td>-0.1</td>
<td>-0.1</td>
<td>30</td>
</tr>
<tr>
<td>23</td>
<td>8</td>
<td>-0.1</td>
<td>-0.2</td>
<td>-0.2</td>
<td>60</td>
</tr>
<tr>
<td>24</td>
<td>20</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>60</td>
</tr>
<tr>
<td>25</td>
<td>21</td>
<td>0</td>
<td>0</td>
<td>-0.1</td>
<td>60</td>
</tr>
<tr>
<td>26</td>
<td>7</td>
<td>-0.02</td>
<td>-0.02</td>
<td>-0.2</td>
<td>60</td>
</tr>
<tr>
<td>27</td>
<td>14</td>
<td>0</td>
<td>-0.2</td>
<td>-0.2</td>
<td>60</td>
</tr>
<tr>
<td>28</td>
<td>16</td>
<td>-0.1</td>
<td>0</td>
<td>-0.1</td>
<td>30</td>
</tr>
<tr>
<td>Mean</td>
<td>16.0</td>
<td>-0.09</td>
<td>-0.08</td>
<td>-0.12</td>
<td>44</td>
</tr>
</tbody>
</table>
Stereoacuity

The patients with Duane syndrome had reduced stereoacuity compared to the normal group (Tables 1, 2; TNO: mean 75 seconds of arc in the patients compared to 44 seconds of arc in the normal group, \( P < 0.01 \); Titmus: mean 59 seconds of arc in the patients compared to 43 seconds of arc in the normal group, \( P < 0.02 \); Mann-Whitney test).

Contrast Sensitivity

The mean contrast sensitivity functions for the 14 normal subjects are shown in Figure 1A. There is no significant difference between left and right eyes (ANOVA; \( F_{(1,130)} = 0.51; P = 0.47 \), but the binocular enhancement measured by comparing the binocular contrast sensitivity to the mean of the two monocular contrast sensitivities is highly significant (ANOVA; \( F_{(1,130)} = 12.72; P < 0.0001 \)). Mean contrast sensitivity functions for the 14 patients with Duane syndrome are shown in Figure 1B. The small difference between the monocular functions for the affected and fellow eyes is not statistically significant (ANOVA; \( F_{(1,130)} = 1.79; P = 0.18 \)), but the binocular enhancement compared to the mean of the monocular contrast sensitivities is highly significant (ANOVA; \( F_{(1,130)} = 25.34; P < 0.0001 \)).

The binocular enhancement of contrast sensitivity in the patients with Duane syndrome was significantly greater than in the normal subjects, both in relation to the mean and the best monocular contrast sensitivities (Fig. 2A). The mean ratio of binocular-to-mean monocular contrast sensitivity across spatial frequencies is 1.52 for the patients compared to 1.33 for the normal subjects (\( F_{(1,130)} = 7.87; P = 0.006 \)). The mean ratio of binocular enhancement to the best monocular response across all spatial frequencies is 1.32 in the patients and 1.17 in the normal group (\( F_{(1,130)} = 5.09; P = 0.026 \)).

Overall there is no significant difference between the binocular contrast sensitivity functions of patients with Duane syndrome and normal subjects (Fig. 1D; \( F_{(1,130)} = 0.053; P = 0.82 \)). The monocular contrast sensitivities of the affected eyes of the patients are significantly worse than those of the left eyes of the normal subjects (\( F_{(1,130)} = 4.77; P = 0.031 \)). The difference between the fellow eyes of the patients and the right eyes of the normal group is not significant (\( F_{(1,130)} = 0.0005; P = 0.98 \)).

The patients with Duane syndrome showed a reduction in both monocular and binocular contrast sensitivities at the highest spatial frequencies when compared to the normal subjects. The mean monocular contrast sensitivity functions are compared in Figure 1C. The difference at the highest spatial frequency is significant (\( t = 3.17, df = 17, P = 0.006 \); unpaired \( t \)-test). The binocular contrast sensitivity functions are compared in Figure 1D. The Duane syndrome subjects are again

![Figure 1](https://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/932904/ on 11/19/2018)
DISCUSSION

Our results confirm previous reports of binocular enhancement of contrast sensitivity in normal subjects\textsuperscript{10,11,14} and extend the finding to patients with Duane syndrome. We have confirmed that patients with Duane retraction syndrome have reduced stereoscopic function\textsuperscript{7}, but surprisingly found an increase in the binocular enhancement of their contrast sensitivities compared to that in normal control subjects. The ratio of 1.33 in normal subjects is slightly less than the ratio of 1.4 reported by Campbell and Green\textsuperscript{10} whereas the ratio of 1.52 in the patients is greater, although both are within the range of values found in the literature\textsuperscript{11}. We found no significant changes in enhancement with spatial frequency, confirming previous findings\textsuperscript{10,14}.

The increase in binocular enhancement came about, not because the patients with Duane syndrome had better binocular contrast sensitivity than normal, but because of a reduction in their monocular contrast sensitivities. The contrast sensitivity of the affected eye of the patients is significantly poorer than that of the control subjects. However, the patients also showed greater binocular enhancement than normal when the binocular sensitivities were compared to the best monocular sensitivity, and the finding was therefore not simply due to changes in the affected eyes of the patients.

Although most patients with Duane syndrome use a head turn to maintain binocular single vision most of the time, there is nevertheless an intermittent misalignment of their eyes that is present during the sensitive period of visual development. It has been shown that there is a loss of binocularly driven cells in the visual cortex in kittens with a surgically induced constant squint\textsuperscript{15} and in monkeys reared with a prism-induced optical dissociation of their eyes\textsuperscript{16}. By analogy with these animal experiments, it is likely that patients with Duane syndrome lose some of their binocularly driven cells during visual development, and, indeed, some lose binocular function altogether\textsuperscript{7}. A reduction in binocular cells could account for the reduced stereoscopic function, because stereopsis relies on disparity detection by binocularly driven cells. It is suggested that the greater binocular enhancement of contrast sensitivity in these patients could also be explained by their having fewer binocularly driven neurons. Whereas stereoscopic function depends on binocularly driven cells, it is likely that both monocularly and binocularly driven cells can be used for the contour recognition involved in our contrast sensitivity task, provided that sensory fusion is present. The total number of cortical cells available under binocular conditions (binocular plus monocular for each eye) would therefore be the same in the patients and normal subjects. However, under monocular conditions, only binocular cells plus monocular cells driven by the open eye would be available (Fig. 3). This monocularly available population is smaller in patients with Duane syndrome than in normal subjects, particularly in the affected eye. Thus, fewer cells are available to detect the stimulus contours at contrast threshold, with less availability of spatial and probability summation across the extent of the stimulus. This could reduce monocular contrast sensitivities. Under binocular conditions the increased pool of monocular cells related to the other eye can be recruited, giving increased binocular enhancement and normal binocular contrast sensitivity.

The same model can also explain the increase of monocular contrast sensitivity to be indistinguishable from normal binocular values in patients with an eye enucleated during early visual development, with the whole cortical neuronal population becoming available to the remaining eye\textsuperscript{17,18}.

It is recognized that this explanation is an oversimplification and ignores such factors as possible interocular suppression and the increased activation of binocular cells under binocular conditions compared to monocular, both of which tend to increase binocular enhancement. It nevertheless provides an explanation for the apparently paradoxical combination of reduced stereoscopic function and increased binocular enhancement of contrast sensitivity in these patients. A similar increase in binocular enhancement of contrast sensitivity has recently been described in patients with microtropias and

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure2.png}
\caption{(A) Binocular enhancement of contrast sensitivity to the mean monocular value at different spatial frequencies in patients with Duane syndrome compared to normal subjects. (B) Mean ratios of contrast sensitivity for affected eye to normal left eye and fellow eye to normal right eye and binocular contrast sensitivities for patients compared to normal subjects.}
\end{figure}

significantly worse at the highest spatial frequency ($t = 2.55$, $df = 17$, $P = 0.021$; unpaired t-test). The ratios of mean contrast sensitivity of the patients to the normal subjects, comparing affected eyes with normal left eyes and fellow eyes with normal right eyes, and the binocular contrast sensitivities are plotted in Figure 2B. This confirms the presence of a generalized relative reduction of contrast sensitivity in patients with Duane syndrome at the highest spatial frequency.
anomalous binocular single vision, and the same explanation may well apply. If this explanation of changes in monocularly and binocularly available populations is applicable, then parallel changes may be present in monocular and binocular electrophysiological testing. A companion article describes electrophysiological experiments that test this possibility in a similar group of patients with Duane syndrome.

References