Sparing of coarse stereopsis in stereodeficient children with a history of amblyopia

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Introduction

It is widely recognized that stereoscopic depth percepts result from small retinal disparities within Panum’s fusional area (Panum, 1858/1940). Less recognized is the fact that reliable depth information is also provided by large disparities that cannot be fused and produce double vision (Ogle, 1952). We reported recently that stereopsis in the diplopic (coarse) range matures by 4 years of age, but stereopsis in the fusible (fine) range, at least for small disparities, continues to mature into the school-age years (Giaschi, Narasimhan, Solski, Harrison, & Wilcox, 2013). Here we test the possibility that the early development of coarse stereopsis makes it resilient to the factors that cause amblyopia.

Fine versus coarse stereopsis

The existence of a “coarse” disparity processing mechanism was studied in early investigations of stereopsis (Mitchell, 1969; Ogle, 1953; Tschemerack & Hoefer, 1903) but remains poorly understood. More recently, Wilcox and Hess (1995, 1996, 1997, 1998) showed that different neural mechanisms seem to support fine (first-order) and coarse (second-order) stereopsis. This distinction is upheld by other physiologists (Hess & Wilcox, 1994, 2008; Kovacs & Feher, 1997; Langley, Fleet, & Hibbard, 1999; Lin & Wilson, 1995; McKee, Vergheze, & Farell, 2004, 2005; Sato & Nishida, 1994; Schor, Edwards, & Sato, 2001; Wilcox, 1999) and physiological (Tanaka & Ohzawa, 2006) research. These studies typically present very different stimuli to each eye, forcing the visual system to extract a disparity signal from the stimulus envelope and to ignore the interior detail. Following the convention in the motion literature, Wilcox and Hess (1995, 1996) refer to stereopsis based on the luminance detail as first order and to that relying on the overall envelope as second order. In addition, second-order stereopsis is robust to large interocular differences in detail and luminance and provides depth estimates for stimuli at the upper limit of disparity processing (Wilcox & Hess, 1995) or for stimuli with ambiguous matches in the two eyes. Here we link this second-order system with coarse stereopsis and relate first-order stereopsis, which is highly sensitive to the similarity of the images in the two eyes and provides very precise depth estimates, with fine stereopsis.

Typical development of stereopsis

Stereopsis is not present at birth but appears by approximately 4 months of age in most human infants (Birch & Petrig, 1996; Birch, Shimojo, & Held, 1985; Fawcett, Wang, & Birch, 2005; Shea, Fox, Aslin, & Dumais, 1980; Takai, Sato, Tan, & Hirai, 2005). Binocular fusion follows a similar time course (Birch & Petrig, 1996; Birch et al., 1985). Most previous studies of the maturation of stereopsis have used commercially available tests, such as the Titmus, Randot, Frisby, or TNO. Estimates of the age at which stereoaucity reaches adult levels vary considerably and depend on the test used; however, most studies agree that stereoaucity is still immature at 5 years of age and reaches adult levels between 6 and 9 years of age (Ciner, Scheiman, Schanel-Klitsch, & Weil, 1989; Cooper, Feldman, & Medlin, 1979; Fox, Patterson, & Francis, 1986; Heron, Dholakia, Collins, & McLaughlan, 1985; Leat, St. Pierre, Hasan-Abadi, & Faubert, 2001; Romano, Romano, & Puklin, 1975; Simons, 1981; Tomaç & Altay, 2000). In contrast, Birch and Petrig (1996) reported that visually evoked potential (VEP) responses to stereoscopic stimuli approached adult levels by 6 to 7 months when assessed using dynamic random dot patterns. Note that the early maturation evident in these VEP results likely reflects the development of binocular cortical circuitry, which is not yet optimally utilized. Birch and Petrig (1996) report a nonmonotonic VEP amplitude versus disparity function with two amplitude peaks corresponding to small and large disparities. These authors refer to disparities greater than 20 arc min as “coarse” because they are large relative to their range of test disparities; however, this is not equivalent to our diplopia-based classification. In fact, while random-dot stereograms are very useful for avoiding the presence of monocular features, diplopia is not perceived in them due to the presence of multiple false matches.

The role of coarse stereopsis in human vision

The distinct response properties of first- and second-order stereopsis likely reflect differences in their roles in depth perception in natural settings. For example, the high resolution and strict matching requirements of the fine stereoscopic system make it ideal for making high-resolution depth judgments, for instance, when threading a needle. The function of the coarse stereoscopic system is still unclear; however, the work of Wilcox and Hess (1996, 1997, 1998) and of McKee and her colleagues (2004, 2005) supports the proposal that these two systems operate in a synergistic manner in adults. That is, the fine system is used when the binocular correspondence is unambiguous, and the coarse system serves as a type of backup mechanism, which is relied upon when the images in the two eyes have different luminance, are ambiguous (e.g., repetitive bars), or are presented at disparities that are well beyond the fusion limit.

Another possible role for coarse stereopsis is in the early development of coordinated binocular eye movements. As summarized by Simons (1993), the developing visual system initially faces enormous calibration challenges and considerable internal noise, which jeopardize its ability to make fine stereoscopic matches. In spite of this, there is considerable evidence that infants are able to converge to binocular targets with latencies as low as 100–200 ms (Tondel & Candy, 2008) with reasonable accuracy (Hainline & Riddell, 1995). Infants under 2 months of age are poorer than adults in both speed and accuracy but improve rapidly, reaching adult levels between 3 and 6 months (see Bobier, Guinta, Kurtz, & Howland, 2000). As outlined above, this is also the age at which “functional” levels of stereopsis are reported. While there is some evidence that the accommodative system can be used to help calibrate vergence responses (Turner, Horwood,
Stereopsis in atypical visual development

Previous studies have found that stereopsis in the fusible range of disparities is often disrupted by strabismus, particularly when the onset is early (e.g., Archer, Helveston, Miller, & Ellis, 1986; Birch & Stager, 1985; Rutstein & Eskridge, 1984). However, there is preliminary evidence for the resilience of stereopsis at larger disparities in adults who have disrupted binocular vision. McColl, Ziegler, and Hess (2000) demonstrated that some individuals who are stereoanomalous are able to localize stimuli in depth via coarse disparity signals. Furthermore, Harris, Wilcox, Moroz-Harris, Day, and Smith (2000) found that a subset of their observers with strabismus were able to judge the relative depth of diplopic targets better than visually normal subjects in spite of the fact that they performed very poorly on standard tests of stereopsis.

Amblyopia is a developmental disorder characterized by poor visual acuity in one eye despite optimal refractive correction. The most common causes are strabismus, a refractive difference between the eyes (anisometropia), or both strabismus and anisometropia that goes untreated for a prolonged period during early childhood. Stereopsis is often disrupted in amblyopia, particularly with strabismus (Asper, Crowther, & Crowther, 2000; McKee, Levi, & Movshon, 2003). However, conventional clinical tests of stereopsis use only disparities in the fusible fine range (0.66 to 13.0 min of arc); therefore, the status of coarse stereopsis in amblyopia is not known.

Amblyopia usually develops after 6 months of age but not after 8 years of age (von Noorden, 1990), a time period when fine stereopsis is still maturing. It is important to note that there are different sensitive periods for different aspects of vision (reviewed in Lewis & Maurer, 2005). For example, the sensitive period for both the typical development of and damage to motion-defined form perception ends earlier for fast motion than for slow motion (Hayward, Truong, Partanen, & Giaschi, 2011). These results support the “Detroit model,” which asserts that different structures and functions are susceptible to disruption at different times and that structures and functions that mature earlier are less susceptible to damage than those that develop later (Levi & Carkeet, 1993). Although we do not know the exact age of maturation of the neural substrate that processes coarse disparities, our recent results suggest that it is before 4 years of age and earlier than the age of maturation for encoding fine disparities. It may develop quite early, before amblyogenic factors have their full effect. Thus, the sparing of large disparities in amblyopia may be additional evidence for the early development of a coarse stereoscopic mechanism with an important role in the development of binocular vision. The purpose of the current study is to investigate the possible sparing of stereopsis for large, diplopic disparities in children with a history of strabismic, anisometropic, or aniso-strabismic amblyopia and poor stereoacuity.

Methods

Participants

This study adheres to the tenets of the Declaration of Helsinki and was approved by the University of British
Columbia Research Ethics board. Prior to testing, informed consent was obtained from each parent, and verbal or written assent was obtained from each child. Thirty-two children (5 to 12 years of age) who had been treated for strabismic, anisometropic, or aniso-strabismic amblyopia but were no longer undergoing occlusion therapy were recruited from the Ophthalmology Clinic at BC Children’s Hospital. The initial diagnosis of amblyopia (before treatment) was established based on a two-line difference in Snellen acuity between the two eyes (equivalent to 0.2 LogMAR difference) with the best optical correction in place. In addition, the minimum Snellen acuity for the amblyopic eye was 20/32 or worse (equivalent to 0.2 LogMAR); the maximum Snellen acuity for the fellow eye was 20/32 or better. The patient was considered to have anisometropic amblyopia if, in addition to the visual acuity difference, the spherical equivalent difference between the two eyes was at least 1 diopter in the absence of any ocular manifest deviation (Weakley, 2001). Strabismic amblyopia was diagnosed if the patient showed any constant or intermittent manifest deviation ≥1 prism dioptr with an accommodative or nonaccommodative involvement (Pediatric Eye Diseases Investigator Group, 2003). Aniso-strabismic amblyopia was diagnosed if the patient met the criteria for both anisometropic and strabismic amblyopia.

For the present study, distance visual acuity was assessed by the Regan high-contrast letter chart (Paragon Services, Nova Scotia; Regan, 1988). For one child who had not yet mastered the alphabet, the Lighthouse symbols chart was used to assess visual acuity (Lighthouse Low Vision Products). Stereoacuity was assessed using the Randot Preschool test (Stereo Optical Co.). Data were excluded from analysis if stereoacuity was better (lower) than 100 arc sec (N = 10) because the purpose of the study was to examine coarse stereopsis in children with clinically poor stereoacuity. Data were also excluded if the child failed to understand the task outlined in the section on depth discrimination (N = 3). Nineteen children with a history of amblyopia were included in the analyses: five with strabismic amblyopia, eight with anisometropic amblyopia, and six with aniso-strabismic amblyopia (Table 1). All 19 children had a fellow eye visual acuity of 0.1 LogMAR or better at the time of testing. There was no visual acuity cutoff for the amblyopic eye. Some of the children had normal visual acuity in the amblyopic eye following treatment, and others did not.

The data of 19 control children with normal vision (Giaschi et al., 2013) to match the age range of the children in the amblyopia group. All children in the control group had best corrected visual acuity of at least 0.1 LogMAR on either the symbols chart (N = 3) or the Regan chart (Chen, Chandna, Norcia, Pettet, & Stone, 2006; Dobson, Clifford-Donaldson, Green, Miller, & Harvey, 2009), stereoacuity of 60 arc sec or better on the Randot Preschool test, and no ocular pathology.

**Apparatus**

The stimuli were generated using a Macintosh G4 computer and presented on a ViewSonic Graphic series G225f CRT monitor with a resolution of 1024 × 768 and a refresh rate of 120 Hz. Stereoscopic images were displayed through liquid crystal shutter glasses (Crystal Eyes 4) synchronized to the computer. Participant responses were collected using a Gravis game pad pro controller, and the room was diffusely illuminated to avoid glare on the monitor.

**Stimulus**

The display subtended 21.5° × 16.5° at a viewing distance of 1 m. The stimulus was a grey-scale Pokémon character selected at random from a bank of nine characters presented at the center of the display and surrounded by a rectangular, zero-disparity reference frame. Two small, black, zero-disparity squares were positioned above and below the reference frame to aid fusion (see Figure 1). The width of the Pokémon stimuli was fixed at 2.2° while the height varied from 1.6° to 3.1° according to the character. To maintain a fixed distance of 0.6° between the outside edge of the stimulus and the reference frame, the width of the frame was scaled with the test disparity while the height varied with the character. Test disparities of 0.02°, 0.08°, 0.17°, 0.33°, 0.67°, 1.0°, 2.0°, 2.5°, 3.0°, and 3.5° were used.

**Procedure**

**Measurement of the diplopia point**

We began with an experiment to separate the disparity range into fine and coarse regions based on a quantitative measure, that is, the proportion of trials in which the stimuli appeared fused (vs. diplopic; Wilcox & Hess, 1995). Participants were initially instructed using an animated PowerPoint presentation (to explain the task) to indicate whether they saw one or two characters. At the beginning of each trial, a happy face image appeared for 500 ms to ensure fixation was at the zero-disparity plane. The Pokémon character was visible for 320 ms (the shortest duration that children would tolerate in pilot studies), and trials were self-paced. A midrange subset of the test disparities was used and presented randomly in each trial as crossed or
<table>
<thead>
<tr>
<th>Age (years)</th>
<th>LogMAR VA at testing AE</th>
<th>LogMAR VA at testing FE</th>
<th>Amb type</th>
<th>Stereoacuity (arc sec)</th>
<th>Treatment history</th>
<th>Strabismus type</th>
<th>LogMAR VA at diagnosis AE</th>
<th>LogMAR VA at diagnosis FE</th>
<th>Optical correction at diagnosis AE</th>
<th>Optical correction at diagnosis FE</th>
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<tr>
<td>5.93</td>
<td>0.2 (RE)</td>
<td>0.1</td>
<td>Strab</td>
<td>800</td>
<td>Surgery, OT: 8 months</td>
<td>Partial accom. ET</td>
<td>0.7 (RE)</td>
<td>0.2</td>
<td>RE: +4.25/+1.75 × 065</td>
<td>LE: +3.50/+2.00 × 105</td>
</tr>
<tr>
<td>7.64</td>
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<td>0.1</td>
<td>Strab</td>
<td>800</td>
<td>Surgery, OT: 10 months</td>
<td>Partial accom. ET</td>
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<td>LE: +8.00/+1.00 × 080</td>
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<td>0</td>
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<td>&gt;800</td>
<td>Surgery, OT: 41 months</td>
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<td>0.2</td>
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<td>0.1</td>
<td>Strab</td>
<td>&gt;800</td>
<td>Surgery</td>
<td>Accom. ET</td>
<td>0.4 (RE)</td>
<td>0</td>
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<td>LE: +3.75/+2.50 × 095</td>
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<td>0</td>
<td>Strab</td>
<td>&gt;800</td>
<td>OT: 24 months, atropine</td>
<td>Partial accom. ET</td>
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<td>0.1</td>
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<td>0.1</td>
<td>Aniso-strab</td>
<td>&gt;800</td>
<td>Surgery, OT: 16 months</td>
<td>Partial accom. ET</td>
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<td>0</td>
<td>RE: +3.75</td>
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<td>OT: 5 months, atropine: 22 months</td>
<td>Accom. ET</td>
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<td>0.2</td>
<td>RE: +4.50/+0.50 × 090</td>
<td>LE: +6.50/+1.00 × 090</td>
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<td>−0.1</td>
<td>Aniso-strab</td>
<td>&gt;800</td>
<td>OT: 13 months</td>
<td>Accom. ET</td>
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<td>0</td>
<td>RE: +2.00</td>
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<td>Aniso-strab</td>
<td>&gt;800</td>
<td>OT: 39 months</td>
<td>Accom. ET</td>
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<td>0</td>
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<td>LE: +2.00/+3.50 × 075</td>
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<td>Aniso-strab</td>
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<td>Surgery, OT: 26 months</td>
<td>Partial accom. ET</td>
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<td>RE: +7.50/+2.00 × 080</td>
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<td>0</td>
<td>Aniso-strab</td>
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<td>OT: 20 months</td>
<td>XT</td>
<td>0.6 (LE)</td>
<td>0</td>
<td>RE: plano</td>
<td>LE: +2.25/+0.25 × 080</td>
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<td>0.4 (LE)</td>
<td>0</td>
<td>Aniso</td>
<td>400</td>
<td>OT: 8 months</td>
<td>-</td>
<td>0.6 (LE)</td>
<td>0.1</td>
<td>RE: plano</td>
<td>LE: +5.75</td>
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<tr>
<td>6.96</td>
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<td>−0.1</td>
<td>Aniso</td>
<td>100</td>
<td>OT: 17 months</td>
<td>-</td>
<td>0.5 (LE)</td>
<td>0</td>
<td>RE: +0.50</td>
<td>LE: +3.25/+0.50 × 090</td>
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<td>0.1</td>
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<td>800</td>
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<td>-</td>
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<td>RE: +1.00</td>
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<td>−0.1</td>
<td>Aniso</td>
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<td>-</td>
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<td>LE: +3.25/+0.75 × 095</td>
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<td>−0.1</td>
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<td>&gt;800</td>
<td>OT: 48 months</td>
<td>-</td>
<td>1 (LE)</td>
<td>0</td>
<td>RE: plano</td>
<td>LE: +7.75</td>
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<td>11.34</td>
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<td>0.1</td>
<td>Aniso</td>
<td>100</td>
<td>OT: 12 months</td>
<td>-</td>
<td>0.4 (RE)</td>
<td>0</td>
<td>RE: −2.75/+5.50 × 100</td>
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<td>Aniso</td>
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<td>OT: 36 months</td>
<td>-</td>
<td>1 (LE)</td>
<td>0</td>
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<td>0</td>
<td>Aniso</td>
<td>100</td>
<td>OT: 14 months</td>
<td>-</td>
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<td>RE: +2.00/+0.50 × 090</td>
<td>LE: +0.50/+0.50 × 090</td>
</tr>
</tbody>
</table>

uncrossed (0.08°, 0.17°, 0.33°, 0.67°, 1.0°, 2.0°, and 3.0°). Each participant completed a total of 70 trials, 10 per disparity.

Depth discrimination

In the main experiment, the task was to indicate whether the Pokémon character appeared to be in front of or behind the reference frame. Again, an animated PowerPoint presentation was first used to explain the task, and the full set of 10 disparities was used. Each participant completed a block of 20 practice trials with auditory feedback to ensure they could perform the task. This was followed by 20 trials per disparity without feedback, separated into shorter blocks to permit rest breaks.

Results

Diplopia assessment

The “proportion diplopic” as a function of disparity data were fit with a Weibull function to obtain the diplopia threshold (63% diplopic point; Strasburger, 2001). The average diplopia threshold for the control and amblyopia groups is shown in Figure 2. The diplopia threshold occurred between 1° and 2° of disparity and was not significantly different between the groups, \( t(33) = -0.272, p = 0.788 \).

Dividing the amblyopia group into anisometropic, strabismic, and aniso-strabismic subtypes (Figure 3) did not change the results of this analysis, \( F(3, 31) = 0.516, p = 0.675 \). Based on these results, the disparities for the remaining analyses were divided into two sets: fine (0.02°, 0.08°, 0.17°, 0.33°, 0.67°, and 1.0°) and coarse (2.0°, 2.5°, 3.0°, and 3.5°).

Depth discrimination

The mean proportion correct as a function of disparity in the fine range is shown in Figure 4. A repeated measures ANOVA showed main effects of Group, \( F(1, 36) = 24.17, p < 0.0001 \); large effect size, \( f = 0.82 \) (Cohen, 1992) and Disparity, \( F(5, 180) = 10.36, p < 0.0001 \); large effect size, \( f = 0.536 \). This was qualified by a significant Group × Disparity interaction, \( F(5, 180) = 2.72, p = 0.021 \); medium effect size, \( f = 0.274 \). This analysis was followed by tests of the simple effect of Group at each Disparity that showed a main effect of Group at all disparities in the fine range \( (p < 0.05) \).

The mean proportion correct as a function of Disparity in the coarse range is shown in Figure 5. A repeated measures ANOVA showed no main effect of Group, \( F(1, 36) = 1.106, p = 0.30 \), or Disparity, \( F(3, 108) = 0.721, p = 0.541 \); and no Age × Disparity interaction, \( F(3, 108) = 1.237, p = 0.30 \). To determine if our results depended on the etiological subtype of amblyopia, the amblyopia group was divided into anisometropic, strabismic, and aniso-strabismic subgroups (Figures 6 and 7). In the fine range, a repeated measures ANOVA showed a main effect of Group, \( F(3, 34) = 12.04, p = < 0.001 \); large effect size, \( f = 0.82 \) (Cohen, 1992).
effect size, $f = 1.003$, and a main effect of Disparity, $F(5, 170) = 6.17, p < 0.001$; large effect size, $f = 0.427$. This was qualified by a significant Group $\times$ Disparity interaction, $F(15, 170) = 2.16, p = 0.010$; large effect size, $f = 0.436$. This analysis was followed by tests of the simple effect of Group at each Disparity, which showed a main effect of Group at all disparities in the fine range ($p < 0.05$). Tukey’s honestly significant difference was used to examine differences among groups. At the smallest disparity ($0.02^\circ$), controls performed significantly better than all groups of children with amblyopia ($p < 0.01$), and the amblyopia groups showed no significant difference in performance ($p > 0.05$). At a disparity of $0.08^\circ$, controls performed significantly

Figure 3. The proportion of stimuli perceived as diplopic by control ($N = 18$) and amblyopia groups as a function of disparity. Here the amblyopia group is divided into anisometropic ($N = 8$), strabismic ($N = 5$), and aniso-strabismic ($N = 6$) subtypes. Error bars represent the standard error of the mean.

Figure 4. Depth discrimination accuracy as a function of disparity in the fine range for the two groups of children. Error bars represent the standard error of the mean.

Figure 5. Depth discrimination accuracy as a function of disparity in the coarse range for the two groups of children. Error bars represent the standard error of the mean.
Figure 6. Depth discrimination accuracy as a function of disparity (fine range) for the four groups of children. Error bars represent the standard error of the mean.

Figure 7. Depth discrimination accuracy as a function of disparity (coarse range) for the four groups of children. Error bars represent the standard error of the mean.
better than all groups of children with amblyopia \((p < 0.01)\), the anisometropic amblyopia group performed better than the strabismic or aniso-strabismic amblyopia group \((p < 0.01)\), and the strabismic and aniso-strabismic amblyopia groups showed no significant difference \((p > 0.05)\). At a disparity of 0.17°, controls performed significantly better than all amblyopia groups \((p < 0.01)\), the anisometropic amblyopia group performed better than the strabismic or aniso-strabismic amblyopia group \((p < 0.01)\), and the strabismic amblyopia group performed better than the aniso-strabismic amblyopia group \((p < 0.01)\). At a disparity of 0.33°, controls performed significantly better than all amblyopia groups \((p < 0.01)\); the anisometropic and strabismic amblyopia groups showed no significant difference \((p > 0.05)\) but performed significantly better than the aniso-strabismic amblyopia group \((p < 0.05)\). At the largest disparities in the fine range \((0.67°, 1.0°)\), the control and anisometropic amblyopia groups showed no significant difference in performance \((p > 0.05)\), both groups performed better than the strabismic or aniso-strabismic amblyopia groups \((p < 0.01)\), and there was no significant difference between the strabismic and aniso-strabismic amblyopia groups \((p > 0.05)\).

In the coarse range \((\text{Figure } 7)\), a repeated measures ANOVA showed no main effect of Group, \(F(3, 34) = 2.15, p = 0.112\); large effect size, \(f = 0.44\), or Disparity, \(F(3, 102) = 0.469, p = 0.704\), and no Group \times\ Disparity interaction, \(F(9, 102) = 1.00, p = 0.445\). Because the mean performance of the aniso-strabismic group was consistently lower than that of the other three groups, a post hoc power analysis was conducted to determine if our design had enough power to detect a Group effect. The power of the Group effect with our sample size of 38 was only 0.50. On the basis of the Group effect size \((f = 0.44)\) and the recommended power of 0.80 \((\text{Cohen, 1992})\), an \(N\) of approximately 17 per group \((68\ \text{total})\) would be required to obtain a significant Group effect at the .05 level.

### Additional analyses

Correlation and multiple regression analyses were used to examine the relationship between depth discrimination accuracy and several clinical measures for participants in the amblyopia group. An average fused and an average diplopic accuracy was determined for each child. When stereoacuity was not measurable on the clinical test \((>800; \text{Table } 1)\), it was assigned a value of 1,200 for these analyses. Although all children had poor stereoacuity, those with better stereoacuity showed higher accuracy for both fused \((r = -0.827; p < 0.001)\) and diplopic \((r = -0.560; p = 0.013)\) stimuli. Amblyopic eye visual acuity at the time of testing was significantly correlated with fused \((r = -0.475; p = 0.040)\) but not with diplopic \((r = -0.418; p = 0.075)\) stimuli. For both fused and diplopic stimuli, neither the amblyopic eye visual acuity change due to treatment nor the amblyopic eye visual acuity at the time of initial diagnosis was correlated with task performance \((\text{all } ps > 0.105)\).

For fused stimuli, stereoacuity was a significant predictor \((\beta = -0.785, p < 0.001)\), and visual acuity was not a significant predictor \((\beta = -0.084, p = 0.609)\) of depth discrimination; the model accounted for 65% of variance in fused performance, \(F(2, 16) = 17.687, p < 0.001\). For diplopic stimuli, however, neither stereo-acuity \((\beta = -0.468, p = 0.063)\) nor visual acuity \((\beta = -0.185, p = 0.441)\) was a significant predictor of depth discrimination; although statistically significant, \(F(2, 16) = 4.112, p = 0.036\), the model accounted for only 25.7% of variance in diplopic performance.

At the time of testing, the visual acuity in the amblyopic eye had recovered to within normal limits in seven children and continued to meet our definition of amblyopia in 12 children. A repeated measures ANOVA followed by pairwise comparisons revealed higher discrimination accuracy at the two finest disparities \((p < 0.01)\) in the children who had recovered from amblyopia. There was no difference between these two groups of children at larger disparities \((p > 0.05)\). This is consistent with the correlation between amblyopic eye visual acuity and depth discrimination accuracy in the fused range only.

### Discussion

Our results suggest that stereopsis for large disparities that produce diplopia may be spared in children with disrupted binocular vision due to amblyopia. Using a two-alternative forced-choice depth discrimination task, we found that children with a history of strabismic or anisometropic amblyopia with poor stereoacuity achieved above-chance accuracy equal to that of controls with normal stereopsis at disparities that were outside Panum’s fusional area. These same children showed markedly poorer performance relative to controls for smaller disparities that could be fused, particularly when the amblyopia was associated with strabismus. The latter finding is not surprising given that these children were selected on the basis of their poor stereoacuity. In addition, although this is the first assessment of stereopsis in amblyopia across such a large range of disparities, stereoscopic deficits for small disparities, particularly in strabismic amblyopia, are well documented \((\text{Simons, 2005})\). Children in the anisostrambic amblyopia group performed at close to chance levels at all disparities. The division of our
amblyopic group into subtypes resulted in a reduction of statistical power; therefore, additional testing is required to evaluate the relative performance of the three amblyopic subtypes. The correlation and multiple regression analyses suggest that the extent of binocular disruption as assessed by clinical measures of stereo-acuity is related to the degree of spared stereopsis but mainly for fused disparities. Visual acuity in the amblyopic eye showed a weaker relationship to the degree of spared stereopsis and in the fused range only.

**Developmental implications**

We recently reported that stereopsis is typically mature for large disparities by the age of 4 years, and stereopsis for smaller disparities is still developing (Giaschi et al., 2013). In line with this finding, the present results could reflect the earlier maturation of stereopsis for coarse disparities (outside of Panum’s fusional area) relative to stereopsis for fine disparities (within Panum’s area). Because amblyopia is not present at birth, aspects of vision that mature earlier may be less susceptible to disruption than those that develop later (Levi & Carkeet, 1993; Lewis & Maurer, 2005). However, we do not know the exact age of typical maturation for coarse disparities, and we do not have accurate information about the age of amblyopia onset in our participants. Our results are consistent with the Detroit model presented in the Introduction (Levi & Carkeet, 1993).

**Fine versus coarse stereopsis**

There has been debate in the literature as to whether fine and coarse stereoscopic processing fall along a continuum or reflect the operation of two distinct mechanisms. Some authors have supported the presence of a continuum of essentially identical disparity detectors that process the full range of fine to coarse disparities (Richards & Kaye, 1974). However, this work is also consistent with a large body of research that suggests there are two distinct populations involved (Hess & Wilcox, 1994; Mitchell, 1969; Ogle, 1953; Schor & Wood, 1983). For instance, Jones (1977) provided strong support for a distinct coarse disparity mechanism when he showed that observers with substantial deficits in processing large disparities typically performed at normal levels when presented with small depth offsets.

In the Introduction, we linked fine stereopsis with a first-order stereo system that is highly sensitive to the similarity of the images in the two eyes and provides very precise depth estimates. We linked coarse stereopsis with a second-order stereo system that prevails when luminance details are unreliable, ambiguous, or diplopic (McKee et al., 2004, 2005; Wilcox & Allison, 2009). It is tempting to conclude that the present findings reflect a spared second-order system that continues to function when the first-order system has been disrupted during development. This is particularly consistent with the improved performance in the coarse range in the strabismic amblyopia group (Figures 6 and 7). However, the spatially broadband Pokémon stimuli that we used to create a child-friendly assessment tool do not allow us to draw firm conclusions about the mechanisms underlying the spared binocular vision we observed. Further work is required using stimuli whose spatial properties (contrast envelope, spatial frequency content, interocular correlation) can be systematically manipulated.

**The role of suppression**

In amblyopia, binocular single vision is maintained in the absence of fusion by persistent suppression of the visual input from the amblyopic eye by the fellow eye and selective enhancement of the input from the fellow eye (Harrad, Sengpiel, & Blakemore, 1996; Sireteanu, Fronius, & Singer, 1981; von Noorden, 1985). Suppression provides a fundamental limit to the extent to which information from the amblyopic and fellow eye can be combined. In a recent study, we found that the amount of suppression was directly proportional to the degree of stereoacuity loss and that there was greater interocular suppression in children with strabismic amblyopia and/or poor stereoacuity (Narasimhan, Harrison, & Giaschi, 2012). Although the group differences in diplopia threshold and depth discrimination accuracy in the coarse range in the current study were not significant, it is notable that the children with aniso-strabismic amblyopia consistently performed more poorly than children in the other three groups (see Figure 7). While these children did not report suppression of an image, and we did not measure interocular suppression, it remains possible that their reduced accuracy may be due to suppression of the amblyopic eye by the fellow eye; this possibility requires further investigation.

**Neural correlates**

McKee and colleagues (2003) suggested that two distinct developmental anomalies account for the pattern of spatial vision loss in amblyopia. Monocular blur with concordant visual input during development as occurs with anisometropia (or with intermittent strabismus) leads to a selective loss of neurons tuned to high spatial frequencies but no loss of binocular
neurons in V1. On the other hand, discordant visual input during development as occurs with misalignment of the eyes (or with severe anisometropia) leads to a loss of binocular neurons followed by a reorganization of V1. The disrupted binocular connections rearrange to drive the remaining monocular cells. We suggest that binocular neurons in extra-striate cortex with larger receptive fields may be less sensitive to discordant visual input and that these neurons could support coarse stereopsis. Studies of macaque neurophysiology (Uka & DeAngelis, 2006) and functional magnetic resonance imaging in humans (Neri, Bridge, & Heeger, 2004) have implicated the dorsal visual stream, specifically MT/hMT+ as part of the neural substrate underlying coarse disparity processing. The ventral visual stream may be more important for fine disparity processing (reviewed in Roe, Parker, Born, & DeAngelis, 2007) although additional study is required to rule out variables such as task complexity and noise sensitivity.

Clinical significance

Stereoacuity is often disrupted in strabismic amblyopia and spared in anisometropic amblyopia; further, the combined aniso-strabismic subtype is often grouped with the strabismic subtype (e.g., Barnes, Hess, Dumoulin, Achtman, & Pike, 2001; Mansouri, Allen, & Hess, 2005; Narasimhan et al., 2012). It remains unclear, however, whether subtyping based on such amblyogenic factors is useful in terms of understanding these deficits or successfully treating them. Some studies report different patterns of deficits in form and motion perception as a function of treatment required to restore visual acuity may not differ between strabismic and anisometropic amblyopia (Lithander & Sjöstrand, 1991; Stewart, Moseley, Stephens, & Fielder, 2004). Researchers have, therefore, been searching for alternate subtyping schemes to aid in the management and treatment of amblyopia. In the largest study to date (McKee et al., 2003), the factor determining the pattern of visual loss in amblyopia was residual binocular function in the central visual field rather than amblyogenic subtype. This suggests that previous inconsistencies might be due to comparisons across amblyogenic rather than binocularity subtypes of amblyopia. This is particularly problematic given the use of small sample sizes and the fact that some people with anisometropic amblyopia lack binocular vision and some with strabismic amblyopia show residual binocular vision. We suggest that adding coarse stereopsis into the assessment protocol will help clarify the patterns of deficits without requiring the use of larger sample sizes. Our assumption is that some patients with spared coarse stereopsis are currently incorrectly classified as “nonbinocular.”

The amblyopic visual system has recently been shown to be much more plastic than originally believed, and treatment may even be effective into adulthood (Baronecelli, Maffei, & Sale, 2011; Levi, 2012; Maurer & Hensch, 2012; Mitchell & Sengpiel, 2009; Thompson, Mansouri, Koski, & Hess, 2008). There is a recent effort to improve treatment outcomes by employing binocular treatment protocols (Eastgate et al., 2006; Hess, Mansouri, & Thompson, 2010a, 2010b, 2011; Knox, Simmers, Gray, & Cleary, 2012; Mansouri, Thompson, & Hess, 2008; Waddingham et al., 2006). The movement toward treating amblyopia as a disorder of binocular processing makes it imperative that tests of binocularity and stereopsis adequately assess the full range of stereoscopic vision, including coarse processing. It is important to know whether the amblyopic eye is permanently degraded or merely suppressed and capable of functioning if the imbalance between the eyes is removed. In the latter scenario, individuals with residual stereopsis for coarse disparities are potentially more likely to benefit from extensive binocular training regimens.

Conclusion

Children with anisometropic or strabismic amblyopia may have normal stereopsis for large disparities even though stereopsis for small disparities is disrupted. This work is consistent with the presence of a fine/coarse dichotomy in neural processing, but it is not a definitive test of this proposal. Regardless, the fact that residual coarse processing is preserved in children with amblyopia has important clinical implications.

Keywords: amblyopia, depth perception, stereopsis, visual development, psychophysics

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Footnotes

1The Regan chart has LogMAR-type spacing with eight Sloan letters per line instead of five. It was scored by counting the number of letters identified correctly. This was converted to a LogMAR score using the formula $(40 – \text{number of letters identified correctly}) \times 0.0125$.

2The Lighthouse symbols chart has Snellen-type spacing with the symbols house, apple, umbrella instead of letters. It was scored by taking the Snellen ratio of the smallest line on which at least 50% of the symbols were correctly identified. This was converted to a LogMAR score using the formula $–\log (\text{Snellen fraction})$ (Holladay, 1997).

References


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