Vernier Acuity in Down Syndrome

Julie-Anne Little,[1] *J. Margaret Woodhouse,*[2] *Jan S. Lauritzen,*[1] *and Kathryn J. Saunders*[1]

Purpose. Down syndrome (DS) is associated with reduced visual performance. Although poor optical quality has been implicated, no previous data are available regarding the contribution of cortical visual processes. The present study investigated Vernier performance for the first time in children with DS to evaluate the integrity of higher visual processing in this condition.

Methods. Participants were 29 children aged 9 to 16 years who had DS and 68 age-matched developmentally normal children acting as controls. All wore best refractive correction, and none had clinically significant ocular abnormalities. An out-of-phase test-pedestal Vernier stimulus was used to facilitate short test distances and optimize compliance with testing.

Results. Testing was successfully completed by 86% ($n = 25$) of the DS group and 96% ($n = 65$) of the control group. Vernier thresholds were invariant with age in both groups. Mean Vernier acuities were 39.8 arc seconds (SD ± 13.3) and 14.6 arc seconds (SD ± 4.7) in DS and control groups, respectively. When compared with control data, mean Vernier acuity was reduced by a factor of 2.7 in DS.

Conclusions. Vernier thresholds were successfully measured in children with DS and were found to be reduced, indicating that cortical visual function is compromised. Impairment in cortical function in DS may be implicit, relating to histologic reports of differences in the DS brain, or they may result from abnormal experience during visual development. The magnitude of the cortical deficit demonstrated in DS in the present study is significant and should be considered along with previously reported poor optical quality. (*Invest Ophthalmol Vis Sci.* 2009;50:567–572) DOI:10.1167/iovs.08-2250

Persons with Down syndrome (DS) have reduced visual acuity. Ocular abnormalities are more common in DS,[1–6] but this reduction in visual acuity occurs in the absence of any clinically evident ocular conditions.[7–9] Why visual acuity is reduced is not known, but researchers conclude it is not an artifact of subject selection or related to attentional or motivational factors and that an underlying sensory deficit must exist.[8,10] Little et al.[11] investigated the difference between two types of resolution acuity in children with DS between 9 and 16 years of age. Conventional grating resolution acuity was compared with interferometric resolution acuity using behavioral methods. The authors found that children with DS demonstrated substantially poorer thresholds for grating resolution than for interferometric resolution thresholds. This suggests that the optics of the eye play a major role in poor visual performance in DS, whereas retinal function is comparatively closer to normal levels.

It is unclear what role the visual cortex plays on poor visual performance in DS. John et al.[10] compared objective visual acuity measurements recorded with steady state visual-evoked potentials (VEPs) with behavioral clinical visual acuity tests in subjects with DS (9 months to 12.8 years) and age-matched controls (3 months to 14.2 years). Although VEP measures reflect the integrity of the visual pathway to the level of the primary visual cortex, behavioral acuity measures also involve the higher centers of visual and cognitive processing. The investigators found that visual acuity thresholds were significantly lower in the DS subject group for VEP and behavioral measures. Because VEP tests are less cognitively demanding than behavioral tests, this reduction cannot be readily explained by cognitive factors. The authors hypothesized that an underlying sensory defect exists. They compared VEP and behavioral acuity and found that VEP was poorer than behavioral acuity in 89% of the DS group. However, this was also true of most of the control group: 85% of controls demonstrated poorer VEP than behavioral measures of visual acuity. Furthermore, the performance gap between VEP and behavioral acuity in the control group and the DS group was similar. If reduced visual acuity were explained by less efficient or impaired processing beyond the primary visual cortex, one might expect behavioral acuity to be relatively poorer in DS. However, this is not the case, suggesting that the cause of reduced performance lies within the primary visual pathway.

There is some information in the literature regarding cortical development in DS. Histologic reports show differences in the visual cortex of persons with DS.[12–14] Becker et al.[12] reported brain weights in DS subjects significantly lower than in controls after 1 year of age. The authors also found the configurations of cortical layers were less organized in the DS group than in controls. They reported a cessation in growth of dendrites and then dendritic atrophy in the DS group after the first year of life compared with age-matched controls. Delayed myelination in nerve tracts has been reported in DS subjects aged 2 months to 6 years.[15] Takashima et al.[13] investigated histochemical development and aging in subjects with DS and found evidence of poor dendritic maturation and atrophy. It is established that persons with DS have an accelerated aging process (an example is the increased incidence of early senile cataracts) and often demonstrate Alzheimer-type deficits.[16–18]

To investigate acuity related to cortical visual function, the present study used the same participants as those described in Little et al.[11] to investigate Vernier acuity in DS. It is widely accepted that Vernier acuity reflects cortical processing.[19–22] It has been demonstrated, using dichoptic stimuli, that Vernier acuity is processed after the signal inputs have been combined binocularly.[21,23,24] Stanley[25] discussed cortical development in relation to visual function and reported that though grating acuity corresponds to and is limited by retinal ganglion cell density, Vernier thresholds depend more on positional information at a cortical level (see also Fahle and Schmid[26]).

In the present study, careful consideration was given to creating an appropriate Vernier stimulus for use with psycho-

From the [1]Vision Sciences Research Group, Biomedical Sciences, University of Ulster, Northern Ireland, United Kingdom; and the [2]School of Optometry and Vision Sciences, Cardiff University, Cardiff, Wales, United Kingdom.

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Corresponding author: Julie-Anne Little, Vision Sciences Research Group, Biomedical Sciences, University of Ulster, Cromore Road, Northern Ireland BT55 1SA, UK; ja.little@ulster.ac.uk.

physical methods. One obstacle to measuring Vernier acuity is that it is a form of hyperacuity, and the normal human visual system is excellent at detecting a Vernier offset. In view of this, traditional studies of Vernier acuity have used large testing distances. However, this was inappropriate for our subject group, whose attention would be better captured by stimuli at close proximity. A further requirement is that the test be readily explained and simple for all participants to perform. Another desirable criterion was a spatial two-alternative forced-choice (2AFC) technique, which could be performed in a nonverbal manner by the participant if necessary. This made certain types of stimulus configuration inappropriate.

We chose to use a Vernier target similar to the principle of Levi et al.,[27] McKee et al.,[28] and Brown et al.[29] Levi et al.[27] created a test-pedestal stimulus based on a template model, as used in Hu et al.[30] and Levi et al.[31] The stimulus consists of two parts, a test pattern and a pedestal pattern. When the pedestal component is added out of phase relative to the test component, an offset is created and a Vernier task is produced.[30] The change in the local contrast of these two components is assumed to provide the cue for Vernier discrimination.[27] Previously, Morgan[32] and Morgan and Aiba[33] suggested that changes in luminance across a stimulus can produce a barely detectable contrast difference well within the hyperacuity range. The present study aimed to evaluate, for the first time, the Vernier acuity performance of children with DS.

Subjects and Methods

Recruitment and experimental protocols complied with the principles of the Declaration of Helsinki, and ethical approval was granted by local research ethics committees.

Developmentally Normal Subject (Control) Group

The authors were granted permission from the Northern Ireland Education and Library Boards to approach schools for recruitment purposes. A local primary and a local secondary school were contacted, and the principals agreed to send out information leaflets and consent forms to all parents of children 9 to 16 years of age. Written informed consent was obtained from the parents of 71 children (42%). Inclusion criteria were corrected visual acuity better than 0.15 logMAR (6/9 approximate Snellen equivalent) and no history of amblyopia, squint, or ocular disease. Three participants were excluded because they did not meet inclusion criteria, and a report was sent to parents and guardians recommending a full eye examination. The 68 remaining participants ranged in age from 9 to 16 years (mean age, 12.4 ± 1.8 years; 33 boys, 35 girls).

Down Syndrome Subject Group

Participants with DS were members of the Cardiff University Down's Syndrome Vision Research Unit. Children with clinically detectable ocular disease such as keratoconus, cataract, manifested nystagmus, and retinal abnormality, were excluded from participation. All remaining participants 9 to 16 years of age in the cohort were contacted with information regarding the study. Written informed consent was obtained from parents of 29 children (25% of the cohort; mean age, 12.84 ± 1.9 years; 19 boys, 10 girls).

Procedure

Testing for the control group was undertaken in the participants' schools, and the DS group was tested at the School of Optometry and Vision Sciences at Cardiff University. All testing rooms were quiet, and illumination was controlled. The same test apparatus was used across sites, under uniform testing conditions. Each subject's refractive status was assessed using standard distance static retinoscopy, and spectacle correction was worn (when necessary) for all testing. This was applied with the participant's own spectacles, if appropriate, or with trial frames. In accordance with Little et al.,[11] ocular dominance was ascertained for each participant through a typical finger-pointing method based on the Bryngelson technique.[34] Thresholds were subsequently measured using the participant's dominant eye and with the fellow eye occluded.

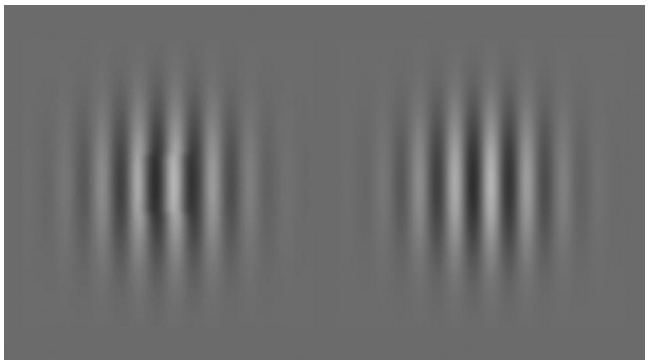

Figure 1. *Left*: Vernier stimulus. *Right*: stimulus without Vernier offset. The contrast has been modified for printing purposes. Within the Vernier stimulus, the target is a small, Gaussian-edged, square grating superimposed on a large Gabor patch mask. The spatial frequency of mask and target is 1.7 cpd. The spatial frequency of the other grating (*right*) is also 1.7 cpd.

Vernier Acuity Measurement

To facilitate the required short working distances, the Vernier acuity task was created using a modified contrast-masking protocol displaying a subpixel offset. The target stimulus was a small sine wave grating (target) superimposed on a large masking sine wave grating (mask). This stimulus is based on McKee et al.[28] and Brown et al.[29] and has been used to measure Vernier acuity in adults and young children (Little J, et al. *IOVS* 2005;46:ARVO E-Abstract 5647).[35] As in Levi et al.,[27] our key assumption was that the change in local contrast introduced by the offset between the target and mask provides the cue for Vernier discrimination. In support of this, Hu et al.[30] concluded that when the target grating is in phase, it is a contrast discrimination task, but when target is 90° out of phase, it is a Vernier task.

The stimulus was a Gabor patch mask with a Gaussian-edged target superimposed centrally 90° out of phase. The out-of-phase target produces a variable Vernier offset in the overall stimulus, depending on the contrast of the target. Both mask and target had a spatial frequency of 1.7 cyc/deg. The Vernier stimulus was displayed spatially beside another grating that did not contain a Vernier offset. The stimulus is shown in Figure 1. The left grating contains the Vernier stimulus. Both sine wave gratings were within a Gaussian envelope and were displayed spatially (Multiscan G500PS; Sony, Tokyo, Japan) with a frame rate of 75 Hz. The stimuli were 16.6 cm apart and 12.2 cm in diameter (512 × 512 pixels). The background was a uniform gray field (14 cd/m^2), luminance matched for the mean luminance of each sine wave grating. A 2AFC QUEST adaptive staircase procedure varied the contrast of the Gaussian-edged target to obtain a detection threshold.[36] This threshold was then expressed as an offset in seconds of arc of visual angle. Generation and control of stimuli were performed using a psychophysics toolbox (MATLAB; The MathWorks, Natick, MA).[37,38]

The participant's task was to indicate which grating contained the Vernier offset, a 2AFC orientation discrimination task. The participant's response was input by the examiner, allowing the next presentation to be displayed. Each trial contained 20 stimulus presentations. The method was thoroughly explained in oral and diagrammatic form. Strengths of the subject with DS included strong visual awareness and visual learning skills and strong motivation to learn by imitating those around him or her.[39–41] Sign language, gesture, and the written word are the best media by which to communicate. Participants, therefore, saw diagrams of the stimuli and were shown which of the sets of lines

was "wavy" or "broken." The participants watched the author perform the task and then were asked to find the wavy or broken lines. To ease identification, each set of stimuli had two cartoon characters beside them. The participants were encouraged to name the character the stimulus was beside, or, if they preferred a nonverbal response, they could point to their chosen stimulus. The terms right and left were not used. All participants were given at least one practice trial before testing commenced to ensure instructions were understood correctly. Stimuli were shown over a long presentation time of 4500 ms, and a trial could be repeated if necessary. Testing distance was 1.5 m for all participants.

Results

Success Rates

Of the 68 control participants, a monocular Vernier acuity measure was obtained from 65 (96%). Of the 29 participants with DS, a monocular Vernier acuity measure was obtained from 25 (86%).

Vernier Thresholds

Figure 2 plots Vernier acuity results for the DS and control groups. Vernier thresholds are expressed in seconds of arc. For both groups, linear regression revealed no significant association between participant age and Vernier acuity. Correlation coefficients for these analyses were: DS group: $r = -0.08$ ($P = 0.69$); control group $r = -0.09$ ($P = 0.48$). Vernier acuity was significantly different between the two groups (one-way ANOVA $F_{(1,88)} = 178.1$; $P = 0$) at the 5% level. The control group demonstrated hyperacute levels of Vernier acuity with a mean acuity of 14.6 seconds of arc; the DS group mean was 39.8 seconds of arc.

Discussion

Vernier acuity was successfully measured in most participants in this study. The data illustrate for the first time that Vernier acuity was significantly reduced in DS subjects compared with developmentally normal controls. Considerable variation was found in the DS data, consistent with previous studies examining visual performance in DS that also showed greater variability in the thresholds of DS subjects than of controls.[7,9,42]

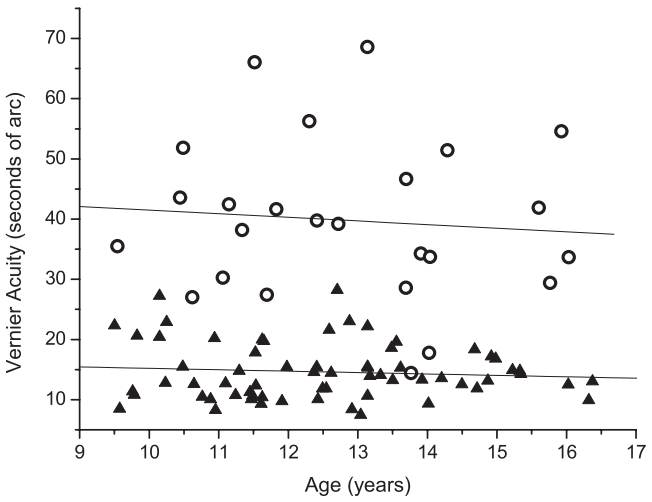

Figure 2. Vernier acuity plotted against participant's age for children with DS (*open circles*) and developmentally normal children (*closed triangles*). Mean Vernier acuity for the DS group is 39.8 seconds of arc (SD ± 13.3). Mean Vernier acuity for the control group is 14.6 seconds of arc (SD ± 4.7). *Solid lines*: linear regressions of the data.

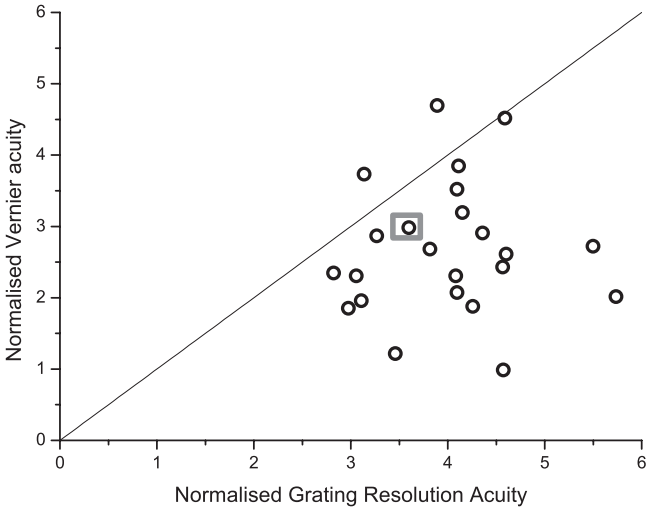

Figure 3. A scatterplot showing the relationship between grating resolution acuity ratio and Vernier acuity ratio for participants with DS. Points represent each participant's acuity relative to the mean acuity in the control group. For example, the *boxed* result indicates that grating resolution acuity was 3.6 times poorer than control mean and that Vernier acuity was 3.0 times worse than control mean for this participant with DS. *Solid line*: line of equality.

The control group demonstrated hyperacute levels of Vernier acuity (mean, 14.6 seconds of arc) in line with those reported in the literature. For example, Gwiazda[43] described adult-like values of Vernier acuity (measured with behavioral methods) of approximately 14 seconds of arc after 8 years of age. More recently, Skoczenski and Norcia[44] reported Vernier acuity (measured with sweep VEPs) of approximately 15 seconds of arc between 10 and 14 years of age. In contrast, DS thresholds fell well below hyperacute levels.

To investigate the relative significance of this Vernier deficit in DS and to examine its contribution to the poor visual performance reported in DS, we compared Vernier thresholds with previously published grating resolution data from the same participants.[11] In contrast to grating resolution acuity thresholds, Vernier responses are relatively insensitive to optical factors, are generated beyond the receptoral level, and are thought to reflect cortical processing mechanisms. Evaluation of the relative impact of DS on grating resolution and Vernier performance may add to our understanding of the contribution of cortical visual processing to visual performance in DS.

Comparison with Resolution Acuities

Although Vernier and grating resolution acuity are often compared in the literature, both represent different visual tasks, and direct comparison of the two measures is questionable. Thus, a ratio of each measure was created to compare with control data,[45] allowing the performance of participants with DS in the Vernier and grating resolution tasks to be directly compared. Little et al.[11] measured interferometric grating resolution acuity and conventional (noninterferometric) grating resolution acuity. Each DS acuity result for noninterferometric grating resolution and Vernier acuity was divided by the control group mean for both measures. Figure 3 plots these normalized values of grating resolution and Vernier acuity for each participant in the DS group. The higher the ratio number (on both axes in Fig. 3), the more degraded the acuity compared with age-matched controls. A ratio of 1 would indicate no

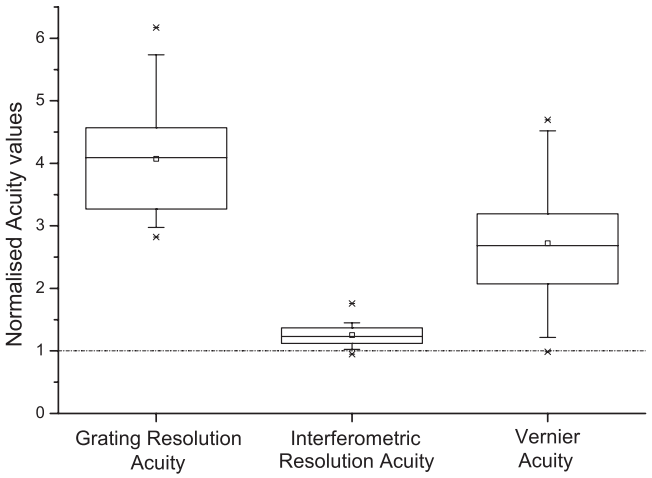

FIGURE 4. Box plots illustrating the profile of each type of DS acuity performance as a ratio of the control group mean. In this figure, the DS data have been normalized and thresholds are described as a ratio of the control mean, identical with the technique used for Figure 3. *Dashed line*: normal level of thresholds derived from control data.

difference between individual DS data and the control group mean.

If Vernier acuity and grating resolution acuity were equally degraded, the points in Figure 3 would fall on the line of equality (the solid line), but for most of the participants tested, the data lay below the line, demonstrating that grating resolution acuity is relatively more degraded than Vernier acuity in children with DS. Vernier acuity in DS participants was, on average, 2.7 times worse than in controls. Grating resolution acuity in DS participants was 4.1 times worse than in controls.[11] Hence, though Vernier acuity was degraded in DS participants compared with control participants, grating resolution acuity was substantially more degraded. By exploring the effect on resolution acuity thresholds of bypassing the optics of the eye, Little et al.[11] argue that optical factors, rather than lack of retinal integrity, can explain the substantial reduction in grating resolution acuity.

Although histologic differences in the cortical architecture of DS brains have been documented, it is unclear what impact these differences have on function. In children with cortical visual impairment, Skoczenski and Good[45] report selective reduction in VEP Vernier acuity compared with VEP grating acuity. Our Vernier data also provide evidence of deficits in cortical processing; however, Little et al.[11] show that optical quality has a substantial influence on visual performance in DS, implying that in DS the cortical deficits in visual processing are augmented by optical degradation of the visual signal.

Little et al.[11] assessed interferometric grating resolution acuity in the same participants with and without DS in the present study. Interferometric grating acuity is measured by bypassing the optical components of the eye and, hence, reflects the integrity of visual processing at the retinal level, without contamination by optical degradation. Comparison of normalized thresholds obtained by grating resolution acuity, interferometric grating acuity, and Vernier acuity in Figure 4 illustrates that interferometric grating acuity thresholds are least degraded in DS, whereas poor optical quality and cortical deficits reduce thresholds elicited by grating resolution acuity and Vernier acuity, respectively.

When comparisons are made between psychophysical thresholds obtained from participants with and without intellectual impairment and a reduction in performance is found in the intellectually impaired group, it is important to consider whether intellectual ability, rather than vision, has influenced the thresholds. To compare Vernier thresholds between children with DS and those without, a Vernier task suitable for children with a range of intellectual abilities was used. Key to this selection was the use of a short test distance and a 2AFC procedure, negating the need for verbal responses and requiring only simple test instructions. The Vernier task had previously been used by the authors to obtain thresholds from developmentally normal children as young as 5 years of age.[35] Both the nature of the test and the success with which thresholds were achieved by most children with and without DS suggested that it was within the cognitive scope of all participants in the present study and that cognitive ability cannot explain the poorer Vernier acuity demonstrated by the DS group. Additionally, all participants with DS in the present study were experienced in vision testing, and, though none had previously attempted the Vernier task, all successfully completed the cognitively challenging logMAR recognition acuity test (involving a 6AFC paradigm) before participation.

To understand the role of Vernier acuity in the poor visual performance noted among children with DS, the present study compared noninterferometric grating resolution acuity data from published data with Vernier thresholds. The authors acknowledge that the techniques used to generate the compared thresholds were not identical; however, they were carefully chosen to be similar in their protocols and cognitive loads. Both tasks were 2AFC, both involved the same number of trials, and both were performed at the same test distance. For both tasks, the participant was required to view two gratings next to each another on a computer screen. In the Vernier task, the participant chose which grating contained the "bendy" or wavy component. This involved the participant assessing both gratings and using their internal representation of "bendy" to match to one of the gratings. In the grating resolution task,[11] the participant had to choose which grating was vertical and to match one of the gratings to their internal representation of vertical. In each case, the participant indicated the choice by pointing or by verbal communication. It is unlikely that the small differences in the Vernier acuity and grating resolution acuity testing paradigms could fully explain the recorded differences in thresholds.

Although it was not possible to use a 2AFC protocol to assess interferometric grating acuity, the task also involved the presentation of horizontal and vertical gratings and required the participant to signal which orientation was seen at each trial. This task involved not only visual memory and processing of internal representations of horizontal and vertical but the subsequent communication of this to the investigator. It may be argued that this task was cognitively the most complex and yet it produced the lowest thresholds, suggesting that the relatively poorer performance of participants with DS in Vernier and grating resolution tasks cannot be attributed to methodological constraints.

It could also be argued that the reduction in Vernier acuity was explained, at least partly, by poor fixation of the DS participants. During testing, the investigator actively encouraged participants to attend to the stimuli to optimize cooperation. Because nystagmus is more common in DS,[46] participants who demonstrated manifest nystagmus by assessment of eye movements were excluded from participation. However, review of participants' clinical records revealed that three participants were reported to have fine-amplitude nystagmus. This was recorded by assessment of image movement on ophthalmoscopy and was not visible by observation of eye movements. To ensure that the presence of fine-amplitude nystagmus could not explain the poorer Vernier acuity thresholds demonstrated by the DS group, the data from these three participants were excluded and reexamined. However, the significant difference between Vernier acuity performance in

DS participants and controls remained (one-way ANOVA $F_{(1,85)} = 156.5$; $P < 0.0001$, at the 5% level; corrected mean Vernier acuity = 39.2 seconds of arc).

Given that significant refractive errors are persistent and often uncorrected in DS when visual acuity is developing, an association between refractive error and Vernier acuity measured in the DS group was considered. Participants were fully corrected for testing, and no significant relationship between refractive error (described by mean spherical equivalent or astigmatism) and Vernier thresholds was present.

Conclusions

This study is the first to measure Vernier acuity in children with DS. The results demonstrated that Vernier acuity is reduced in children with DS compared with age-matched controls. The control group had hyperacute Vernier thresholds consistent with findings in the literature. However, the DS group had significantly poorer Vernier acuity, with thresholds below hyperacute levels.

In a comparison of the present data with those of Little et al.,[11] Figure 4 demonstrates that grating resolution acuity was disproportionately more degraded in DS participants than in controls, with Vernier acuity showing moderate degradation and interferometric grating acuity revealing the least difference in performance. These data suggest that though poor optical quality is an important factor in poor visual performance in DS, processing in the primary visual cortex is also impaired and contributes to the overall deficit in visual function.

The present study further explores the mechanisms underlying reduced visual performance in DS. It is the first to measure Vernier acuity in children with DS and demonstrates a reduction in Vernier acuity compared with that of developmentally normal participants, implying that degradation in cortical visual function exists in DS. Such a deficit could be consistent with histologic reports of differences in the cortex in DS.[12,13] This may be implicit in DS or it may be hypothesized to result from abnormal visual experience during the critical period for visual development. Vernier acuity has been used as a tool to investigate amblyopia, and previous researchers have reported varying degrees of degradation of Vernier acuity in amblyopia, depending on when and how amblyopia arises.[24,47,48] If it were possible to clinically intervene during the critical period in DS, it may also be possible to maximize visual development and to limit any reduction in visual function.

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