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Vision in Down's Syndrome Children

Title:

Refractive Error, Binocular Vision and Accommodation of Children with Down Syndrome

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Abstract

Background

In this review of the visual development of children with Down Syndrome (DS) we were specifically interested in how refractive error, binocular alignment and accommodation are different in DS from the general population. The differences present and their aetiology will help practitioners make informed decisions about the visual assessment and management of these children.

Methods

Articles found using searches through Scopus, Medline and Google Scholar were evaluated by examining sample sizes, appropriate use of controls, methods of measurement and statistical significance of findings. Where the strength of evidence in an article might be weak this is reported in the review.

Conclusion

The development of the visual and oculomotor systems is substantially different in DS compared with the general population. Assessment and optometric management of this special population need to be directed accordingly.

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Down Syndrome (DS) is the most common of the chromosomal abnormalities. The reported incidence of DS ranges from 1 in 600 to 1 in 800 live births.^{1,2} In Australia the incidence is 11 in 10,000.³ DS was first described by John Langdon Down in 1866.⁴ He described the face as "flat and broad... the eyes are obliquely placed... the palpebral fissure is very narrow".⁴ Dr Down established an institution for educating those with intellectual / cognitive disabilities.⁴ DS affects several aspects of the visual system including; refractive error, vision, visual acuity, accommodation and binocular vision (e.g. strabismus). With a comprehensive understanding of how DS affects the eyes and vision, optometrists will be better able to provide more efficient and effective vision care. This review addresses refractive error, binocular vision and accommodation of children with DS. A review of ophthalmic disorders in adults with DS is provided by Krinsky-McHale et al.⁵

It was not until 1932 that P. J. Waardenburg suggested that DS was a disorder caused by an extra chromosome resulting from nondisjunction.⁴ Trisomy 21 represents three copies of chromosome 21 instead of two and is the cause of DS in about 95% of instances. Nondisjunction is the failure of the two parental chromosomes to separate during meiosis. This occurs in the female gamete prior to conception for 76-95% of people with DS.^{6,7} In mosaic DS some of the body's cells have trisomy 21 and others do not. This is due to nondisjunction in one of the early cell divisions of the zygote rather than prior to fertilisation. In about 4% of people with DS the cause is translocation⁸ where an extra portion of chromosome 21 joins onto the tip of another chromosome which is usually chromosome 14.

Systemic Associations

Congenital Heart Defects

Congenital heart defects have been reported in 44.6%⁹ and 47.5%¹⁰ of live births. In both studies the most common defect was atrio-ventricular canal defect. This has been linked to a region on Chromosome 21¹¹ and results in a lack of fusion of two tissues which need to fuse to form a normal atrio-ventricular valve. The average life expectancy of people with DS has been increasing with improvements in healthcare. An

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Australian based study¹² published in 2004 reported the average life expectancy with people with DS to be 60 years of age.

Refractive Error

Difference in type of refractive error

Significant refractive error (spherical equivalent outside of the range of -0.50 to +1.00) is found in almost 80% of children with DS (see Table 1).¹³

Table 1 The prevalence of different types of refractive error for children with Down Syndrome compiled from references.¹³⁻¹⁵

Type of refractive error	Frequency (%)
Hyperopia	
≥ +1.00DS	56
>+2.00 DS	57
≥+0.50DS	80
Myopia	
≤ -0.50DS	18-25
< -0.50DS	12
Emmetropia	
Between -0.50DS and +1.00DS	19
Between or equal to -0.50DS and +2.00DS	32
Between or equal to -0.50DS and +0.50DS	2
Astigmatism ≥ 1.00DC	67-74
Anisometropia ≥ 1.00DS	9-19

Variances in the frequency of refractive error can be partially explained by the difference in definitions used. Doyle et al¹⁵ found 80% of those with DS were hyperopic compared to 56% found by Paudel et al¹³ and 57% found by John et al¹⁴. However Doyle et al¹⁵ defined hyperopia as ≥ + 0.50 DS and Paudel et al¹³ and John et al¹⁴ defined hyperopia as ≥ + 1.00 DS and > +2.0 respectively. Results of Karlica et al¹⁶ and of

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Motley and Saltarelli¹⁷ are similar. Comparison with the general population is not straightforward as prevalence of types of refractive error varies with ethnicity and with age. Prevalence of myopia in children varies from 2% in a Polish study¹⁸, to 5.3% in Australia,¹⁹ 12.3% in Singapore²⁰ and up to 81% in Taiwan.²¹ Hyperopia more than 2.00DS has been reported at 6.1% in Poland¹⁸ and 2.7% in Singapore.²⁰ In Taiwan more than 1.00DC of astigmatism has been reported in 18.4% of children²² and one study found this same level of astigmatism in 36.9% of Hispanic children.²³ Reported prevalence of anisometropia 1.00DS or more in children with DS (9.4%⁸ to 19.4%¹³) is significantly greater to the general population of children (3.4%²⁰ to 5.8%²⁴).

Differences in refractive error over time

At birth there is no significant difference in the prevalence of refractive error between those with DS and controls.²⁵ However Woodhouse et al,²⁵ in a longitudinal study showed that primary-school children with DS had a higher prevalence of significant refractive error (spherical equivalent refractive error more negative than -0.75DS or more positive than +3.0DS) than controls. They also found that for children with DS the prevalence of significant refractive error increased over time and that the spherical equivalent refractive error of primary school children with DS had a larger variability compared with controls.

Table 2 Prevalence of significant error at three levels of development. Results reproduced from Woodhouse et al.²⁵

	Infants	Preschool	Primary School
DS	30%	50%	54%
Controls	25%	5.8%	3.2%

By comparison, for control children aged from infancy to preschool and into primary school, the prevalence of significant refractive error decreased. The trend is that with increasing age, school children with DS have higher rates of significant refractive error.

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The increase in variability of refractive error with age in DS is proposed to occur because of a failure of emmetropisation.^{15, 26}

Aetiology of a failure of emmetropisation

Possible reasons for a failure of emmetropisation include inaccurate accommodation,²⁷ low levels of near work combined with high levels of outdoor activity in children with DS²⁸ and changes in the visual cortex. A large lag of accommodation has been linked to myopia progression, and 55-80%^{29, 30} of children with DS have an abnormally large lag of accommodation. However, hyperopia is more common than myopia in DS¹³ so accommodation cannot explain the failure of emmetropisation in the majority of these children. There is some evidence that outdoor activity and near work can influence a child's refractive error in the work of Rose et al who found that a low level of near work combined with a high number of hours spent outdoors was associated with a more hyperopic spherical equivalent refractive error in their 12 year-old children (+0.56D)²⁸ but this argument is weak because children with DS have not been included in these types of study.

Experiments with chicks lead Troilo et al to conclude that there are both local (within the eye) and cortical components to emmetropisation.³¹ However observations from longitudinal studies of refractive error in individuals with DS have found no evidence of the emmetropisation process occurring.²⁶ Further research is needed to determine why emmetropisation fails in children with DS.

Astigmatism

The prevalence of astigmatism is also especially high in DS. Ljubic et al⁸ found that astigmatism greater than 1.0 DC was present in 74% of a group of 170 people with DS aged between 1 and 34 years and that oblique astigmatism was the most prevalent type (52%). Ljubic et al observed a trend that the incidence of oblique astigmatism increases with age. Al-Bagdady et al²⁶ made the same observations and noted that oblique astigmatism was more prevalent in older children with DS (7.1% of 1 year-olds compared with 30% of 15 year-olds). Al-Bagdady et al found that the J45 component of astigmatism (oblique astigmatism in

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power vector notation) first became statistically significantly different in 7 year-old children compared with 2 year-olds. In the longitudinal arm of their study seven of 12 children developed significant astigmatism and six of the seven developed oblique astigmatism.

Woodhouse et al²⁵ found in her longitudinal study that the frequency of significant astigmatism (1.0DC or more) increased with age. In infants with DS 26% had significant astigmatism, compared to 22% of the same children when they reached preschool age, and 37.5% at primary school age. This strongly contrasts the trend of a reduction in the frequency of astigmatism with age seen in the controls. 48% of the infant controls had significant astigmatism, compared to 15.4% at preschool age and 0% at primary school age. Haugen et al³² also observed the higher prevalence of oblique astigmatism with the correcting cylinder axis being eye specific. Haugen found that 67% of people with DS in the age range 14-26 years had clinically significant (>1.00DC) astigmatism and that 40% of these people had oblique astigmatism. However these authors did not state whether they were using positive or negative cylinder notation. If Haugen et al used negative cylinder notation, the axis-to-eye specificity is consistent with the findings of Al-Bagdady et al where, in those with oblique astigmatism, negative correcting cylinder axis was usually towards 135 degrees for the right eye. Doyle et al¹⁵ used corneal topography results for a group of 15-22 year-olds with DS and confirmed corneal astigmatism directly represented in their overall refractive error and where 38% of eyes had their astigmatic axis outside 10 degrees from orthogonal.

For a group of 100 normal young adults, Read et al³³ found that the J45 corneal astigmatism power vector was significantly correlated to the angle of the palpebral fissure with the angle of the palpebral fissure accounting for 10-25% of the variance of the axis of astigmatism. However, as the number with oblique astigmatism in this group was small (10) any possible link between oblique astigmatism and the oblique palpebral fissures observed in the general population is not strong. However a working hypothesis for DS where the prevalence of oblique astigmatism is greater is that accumulating eyelid pressure at an oblique angle could result in oblique astigmatism and that the increased magnitude of astigmatism which is observed with time represents an accumulation of flattening by the mechanical force of the eyelid.

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The trend of increasing astigmatism over time could partially explain the increase in frequency of significant refractive error over time. It could also be linked to the development of keratoconus. Keratoconus has been reported to be found in 0-15%^{13, 34, 35} of people with DS. However Woodhouse et al²⁵ found that in the 37.5% of primary school age children with DS who had 1.0DC or more astigmatism, none had keratoconus. However, as keratoconus typically develops around puberty, it may be that some of these children went on to develop keratoconus later in life.

The change in astigmatism over time (whatever the cause) is a strong reason for the recommendation that regular eye examinations are important for growing children with DS. The non-correction of significant astigmatism at an oblique angle will reduce vision and will increase the potential for refractive (meridional) amblyopia.

Vision, Visual Acuity and Contrast Sensitivity

Differences in Down Syndrome

For infants with DS under 6 months of age, Courage et al³⁶ found that high-contrast grating acuity measured with Teller cards was within normal limits. However a number of other authors have reported decreased vision in children with DS at older ages.^{36, 37}

Woodhouse et al³⁷ used Cardiff and Teller cards and compared vision in children with DS and age matched controls. The children were aged between 12-weeks and 4.75-years. Vision in the infants under 2 years was not significantly different between children with DS and controls and neither was the spread of the refractive error. In children 2 years old and over, acuity was worse in children with DS and the spread of refractive errors was significantly different between the two groups. However as vision was measured with only with habitual correction and not with current refraction, a decrease in acuity could simply be attributed to uncorrected refractive error. It is also possible that a lower accommodative response in those with DS to the close viewing distances used for some measurements could have reduced performance. The test distances for the Cardiff cards were 50cm or 1m depending on the attentiveness of the child and the

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Teller cards were used at a distance of 38cm. If accommodation was significantly less than the 2.6D, 2D or 1D demanded, then vision measurements would have been reduced.

Little et al³⁸ measured visual acuities for the age range 9-16 years using the crowded logMAR test at 3m. They found a significant difference between children with DS and controls. Refractive error and accommodation were not factors in that study as the children were wearing their current refractive correction and the test distance is within or at the edge of depth of field. The group with DS had a visual acuity of 0.33 logMAR \pm 0.18 (mean \pm standard deviation) (6/13), compared the control group who had a visual acuity of -0.06 logMAR \pm 0.07 (6/5). The conclusion is that although normal levels of vision are found before 6 months,³⁶ the visual acuity of older children with DS compared with controls is decreased.

Clinically when measuring vision of a child with DS, the cognitive abilities of the child should be taken into account. A reduction in visual performance on a standard letter recognition or symbol orientation chart may simply indicate that a preferential looking test is more appropriate for the child. Da Cunha et al³⁹ found that isolated tumbling E methods failed for children with DS and that for these children Teller cards were needed in 85% of those under 5 years of age and for 13% of 5-12 year-olds. None of the children with DS in the 12-18 years of age range required the Teller acuity card as they could all respond to the non-crowded symbol orientation (isolated tumbling E) task.

Courage et al⁴⁰ measured contrast sensitivity across five spatial frequencies in 18 children with DS with ages ranging from 4 months to 14 years. In two 4 month-old infants the resulting spatial contrast sensitivity function (CSF) curve is at the lower limits of, but within the 90% confidence interval of, the normal range. All except two of CSFs of the remaining children fell outside the 90% confidence interval of normal specific to their age. The difference between children with DS and controls generally increased at higher spatial frequencies (finer gratings). Aside from this, the general shape of the CSF was quite similar between the children with DS and the controls. The mean CSF function of the children with DS (mean age 7.3 years) was found to be similar to the CSF of a control 12 month-old child. While a decrease in the accuracy of

accommodative response might be a reason for the reduction in CSF at high spatial frequencies, this cannot explain the generalised decrease at lower spatial frequencies observed in the CSF. These data suggest that at least part of the visual deficit seen in children with DS is cortical in nature. The objective measurements of cortical visual response at a range of spatial frequencies by Suttle and Turner⁴¹ where recordings were less clear from children with Down syndrome than from children with normal development adds evidence to the hypothesis that there is a neural basis for the deficits.

Aetiology of differences in visual performance in Down Syndrome.

A decrease in visual attention could be all or part of the cause of the reduction in measured vision. In those individuals with DS who are more severely cognitively impaired it can be very difficult to attain a reliable measurement of vision. John et al¹⁴ used steady state visually evoked potentials (VEPs) to measure acuity and contrast sensitivity and compared children with DS with age matched controls. These objective techniques required only the child's fixation. Despite the less demanding task, acuity derived from VEP recordings could only be gathered from 62% of children with DS compared with 91% of control children. The measurement failures were when the child did not concentrate on the visual stimuli long enough for sufficient recordings to be taken. In their study they excluded those with inaccurate accommodation so focus errors were not a factor. John et al also measured visual performance using acuity charts chosen according to the child's age and skill level. Behavioural measurements of acuity were better than those derived from VEPs in 89% of children with DS and in 85% of controls. For children with DS acuity derived from VEP was 8.23 ± 3.35 cycles per degree (cpd) (mean \pm standard deviation) [equivalent to 0.56 logMAR or 6/22] compared to their behavioural acuities of 17.37 ± 6.94 cpd [equivalent to 0.24 logMAR or 6/10.5]. The control children's VEP acuity was 11.34 ± 5.95 cpd, [equivalent to 0.42 logMAR or 6/16] compared to their behavioural acuity of 22.65 ± 14.93 cpd [equivalent to 0.13 logMAR or 6/8.1].¹⁴ The comparison is presented in Table 3 which clearly shows that children with DS have a poorer behavioural acuities than age matched controls (difference = 0.11 logMAR or 5½ letters on a logMAR chart) and poorer VEP acuities than age matched controls (difference = 0.14 logMAR or 7 letters on a logMAR chart). If the acuity loss for children with DS had been due solely to decreased attention we would expect there to be a bigger

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difference between behavioural acuity relative to VEP acuity for children with DS, compared to the controls. However, comparing the two groups, the absolute improvement in the vision from VEP to behavioural was approximately equal. This means that in the subset of children with DS who are compliant enough to fixate on a target and have accurate accommodation, decreased attention is not an explanation of their decreased measured visual performance. This decreased acuity can only be explained by either a sensory deficit or a problem in the visual cortex.

Table 3 Comparison of acuity measurements from John et al¹⁴ presented in logMAR units rather than cycles per degree.

	Acuity from		
	VEP	Behavioural	Difference
DS	0.56 (6/22)	0.24 (6/10.5)	0.32 (\approx 3 lines)
Age match controls	0.42 (6/16)	0.13 (6/8)	0.29 (\approx 3 lines)
Difference	0.14	0.11	

Pre or Post Retinal

Acuity measured with interferometric techniques enables the potential resolution limit of the retina to be assessed without influences from pre-retinal structures.³⁸ As the interferometric technique generates grating targets on the retina, interferometric acuity and grating acuity can be compared directly. Both types of acuity were measured in 29 children with DS and controls. Children with DS were found to have a small but statistically significant reduction in interferometric acuity compared with controls. For interferometric acuity the mean result in logMAR units for children (aged 9-16 years) with DS was $+0.003 \pm 0.06$ (6/6) compared with controls -0.11 ± 0.08 (6/4.7).³⁸ This is equivalent to a seven letter difference on a logMAR acuity chart and could be seen as being of little clinical significance; however this small loss of interferometric acuity in children with DS compared to that of the controls does indicate the possibility that there is a small post retinal component to the reduction in vision in DS.

Pre retinal contributions to a reduction in visual acuity could be due to visually significant cataract, or keratoconus. However Courage et al⁴⁰ found that despite a lower contrast sensitivity seen in children with DS, only one child in their study had a small peripheral cataract. None had keratoconus, and all had 1.75DC or less of astigmatism. Little et al³⁸ found that those with DS had a reduced visual acuity compared to controls, and they excluded children with keratoconus or cataracts from their study.

Visual Cortex

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The brain has been shown to be different in people with DS in a number of ways. Takashima et al⁴² examined the cortex of 14 people with DS and controls and found no difference in organisation of the visual cortex between the two groups at 14 to 24 weeks gestation. However by 40 weeks of age, in the normal controls the cells were more ordered and layers were starting to form. Some organisation into layers was seen in the individuals with DS at 4 months of age, however these were still not as ordered as the controls.⁴²

The growth of the dendritic tree structure was also examined in layers 3 and 5 of the visual cortex in eight children with DS and 10 controls.⁴³ The results showed an increase in the growth of the dendritic branch in controls, and a cessation of this growth in DS at about four months of age.⁴³ Dendritic spines in the visual cortex have also been shown to be altered in DS. After 40 weeks of age the number of dendritic spines was lower in DS compared with controls.⁴³ Changes in the dendritic tree structure in the brain in DS have been linked to cognitive ability and "mental deficiency" in DS.⁴⁴ The link between differences in the structure of the visual cortex in DS and the impact this has on the brain's function requires further research.

Although much of the acuity difference after four months appears to be attributable to the optics of the eye, the evidence from measures of interferometric acuity is that a lesser proportion of deficit is due to post-retinal mechanisms. Abnormal organisation of layers in the visual cortex along with decreased dendritic intersections and spines could explain some of the post retinal reduction in vision. It is possible that this cortical deficit may be similar in nature to the deficit seen in amblyopia. The only studies available comparing the visual cortex of those with DS to controls are from the 1980s when magnetic resonance imaging (MRI) was in its infancy. Studies which examine the cortical deficit in amblyopia typically involve more modern MRI scanning techniques^{45, 46} and there are no recent studies available which used MRI scanning to investigate vision in DS. This makes it difficult to conclude whether the neural deficits in the visual cortex are inherent in DS or are simply as a result of refractive amblyopia. If a cortical defect is inherent in children with DS we may be unable to correct it. However if the potential exists for amblyopic

types of cortical defect to develop, then this could perhaps be minimised if focused retinal images were always available.

Accommodation

Difference in Down Syndrome

Accommodative response is reported to be reduced significantly in DS.^{30, 47, 48} The amplitude of accommodation in a young adult without mental disability can be measured with the push up technique. For the push up technique to provide valid measurements the person being examined must have a good level of understanding of the "first sustained blur" end point criterion and be able to cooperate in exerting accommodation effort. This is often not found in children with DS. An objective method of measuring accommodation is usually more appropriate. By measuring the accuracy of accommodation (e.g. lag of accommodation) as the near stimulus to accommodation is increased, the maximum accommodation exerted while a near normal lag of accommodation remains can be estimated objectively. Near targets containing appropriate spatial frequency content must be used so that the acuity of the child is taken into account. The normal lag of accommodation for people with DS should be known so that departures from this level can be detected.

Rouse et al⁴⁹ found the usual mean lag of accommodation in children without DS to be $0.33D \pm 0.35D$. The average working distance at which these measurements were taken was 24.6cm which was the children's mean habitual working distance. A lag of accommodation more than 1D (2 standard deviations from the mean) would be considered abnormal. Using this technique Haugen et al²⁹ found that 55% of children with DS had a lag of accommodation of greater than 1D at working distances of 20-30cm.

Woodhouse et al³⁰ measured amplitude of accommodation in children with DS and control children objectively and used Nott's dynamic retinoscopy to determine the actual lag of accommodation. Firstly, the children's distance refractive error was found using conventional retinoscopy. The children were not corrected for this error during measurements of accommodation but the refraction was taken into account

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in subsequent calculations. A trial frame was not used during measurements to reduce distractions and because using a trial frame on children with DS is not always possible. Accommodative response was measured at three fixation distances: 16.7cm (accommodation demand 6D), 12.5cm (demand 8D) and 11cm (demand 9D). The position of the retinoscope where a neutralised reflex was observed provided the dioptric power of lag or lead of accommodation. The amplitude of accommodation was calculated from taking into account the uncorrected refractive error.

A minor issue of concern with this method is that if there were significant levels of uncorrected astigmatism then the target would be blurred and this blur could have reduced the accommodative response.

Irrespective of this concern, there was a dramatic difference in the amplitude of accommodation measured between controls and the children with DS. Amplitude of accommodation was less than 10D for 7.6% of control children compared with 92% of the children with DS.³⁰ Of the children with DS, 50% had an amplitude of accommodation of 4D or less.³⁰ If we use the clinical guideline that a person can comfortably exert half their amplitude of accommodation during near tasks, then 50% of the children with DS (those with amplitudes of accommodation less than 5D) would need a reading addition for the adult working distance of 40cm. Without an appropriate near correction for their closer working distances, young children with DS may find reading and other school work difficult. An optimum near correction will remove poor near vision as a cause of poor performance at school so that any developmental delay is more accurately measured.

Anderson et al⁴⁸ measured amplitude of accommodation using an objective method for 36 people with DS aged 3-40 years and 140 age matched controls. An open field autorefractor measured accommodation while stimulus to accommodation was incremented with negative lenses. Once no further increase in accommodation was found, the amplitude of accommodation was calculated from the difference between the power of the patient's eyes with the minus lenses and the distance refraction. Those with DS had a mean amplitude of accommodation of $2.52 \pm 1.66D$.⁴⁸ Only 26% of those with DS fell within two standard deviations of the mean of the controls' accommodative amplitude.⁴⁸ The authors suggested that those

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with DS would respond better if a proximal stimulus to accommodation was used. Subsequently, they used a push up technique and found from their measurements the plateau of the stimulus-response function. The response amplitude at which the function flattened was taken as the amplitude of accommodation. Unfortunately mechanical constraints prevented the accommodation stimulus in the autorefractor to move any closer than 12.5cm. At this point 7 of the 19 participants had not reached a plateau in accommodative response and their true amplitude of accommodation could not be found. Anderson et al⁴⁸ also did not use this technique on the controls, which makes it impossible for a comparison to be made.

Aetiology of accommodation differences in DS

The research reviewed shows that the accommodative amplitudes in people with DS are lower than those found for the average population of similar ages, that the magnitude of the deficit probably varies between individuals and that there are difficulties in measuring amplitudes of accommodation objectively. A possible explanation for the lower amplitude of accommodation may be in the mechanics of the crystalline lens. Haugen et al found that the central lens was thinner on average in people with DS; $3.27 \pm 0.29\text{mm}$ compared with controls; $3.49 \pm 0.20\text{mm}$.²⁹ After accounting for the other components of the biometry of the eye, Haugen calculated that the lens power was significantly lower in the DS group; $17.70 \pm 2.36\text{D}$ compared with controls $19.48 \pm 1.24\text{D}$.²⁹ This is a difference of 1.78D. If it is assumed that the mechanics of the lens zonules and ciliary muscle are the same in DS as in the average population, calculations can be made to predict the expected lag of accommodation based solely on the decrease in lens power. The following calculations were made. For a 40cm viewing distance and a 2.50D stimulus to accommodation an average person changes the power of their lens by 12.8% ($2.5/19.48 \times 100$). If a person with DS changes the power of their lens by 12.8% the power of the lens increases by 2.27D. ($17.70 \times 1.12 = 19.97$, $19.97 - 17.70 = 2.27$). Thus the lag of accommodation purely from this decrease in lens power is $2.50 - 2.27 = 0.23\text{D}$. These calculations assume that the percentage change in lens power would be the same between the two groups. This may not be the case as there is evidence that accommodation and vergence are controlled by neural circuits in the form of a defocus feedback mechanism.⁵⁰ This is still however a very small difference in theoretical exerted accommodation between DS and controls.

Another possible explanation for the reduction in accommodation could be that those with DS have a predisposition to earlier presbyopia due to changes within the structure and dynamics of the crystalline lens. Also, the accommodation and vergence neural control mechanism could be different. This involves a number of areas in the brain⁵⁰ and these possibilities need further research and investigation.

Management of accommodation deficits in DS

No matter the aetiology, as optometrists we should investigate if children with DS have reduced accommodation and should manage this appropriately. Bifocal spectacles are an obvious treatment option. Nandakumar and Leat⁴⁷ customised the near addition provided to a group of 14 children with DS. They first provided the children with single vision glasses that corrected their distance refractive error (there were myopes and hypermetropes). After six months of wear they then prescribed bifocals for the child if the lag of accommodation was outside the normal limits described by Leat and Mohr⁵¹ for either a 4D or 6D stimulus to accommodation, whichever was closest to the child's habitual near working distance. The normal limits for the 6-10 year-olds were a lag greater than 0.7D for a 4D stimulus, or greater than 0.8D for a 6D stimulus. For the 11-19 year-olds the limits were a lag greater than 1.12D for a 4D stimulus, or greater than 1.66D for a 6D stimulus. Prior to wear of the distance glasses all children appeared to need a bifocal correction. After 6 months of adaptation two out of fourteen no longer needed one. Nandakumar and Leat suggest using this technique in hyperopes and commented that it is more questionable in myopes, as fully correcting them at distance will make their near work more difficult during the adaptation period.⁴⁷ After 6 months of adaptation and for all children in the study, Nandkumar and Leat introduced positive trial lenses over the distance prescription and until lag of accommodation (measured using dynamic retinoscopy) was within 95% of normal. The working distance chosen for each child was either 16cm or 25cm, whichever was closest to the child's habitual working distance. They found that eleven out of thirteen of the children with DS required a reading addition ranging from +1 to +3.50D. One child dropped out of the study, leaving ten children wearing bifocal lenses.

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The value of the bifocals was assessed by comparing the children's reading grade before and after the bifocals were worn. Nine out of ten children improved their reading grade after one term of using them at school. A few children had exceptional improvements. One child's reading ability moved from grade four to grade six. Another improved from grade two to grade five.⁴⁷ Near visual acuities were measured through the near segment after two weeks of bifocal wear. Significant improvements were found after two weeks of bifocal wear compared with near acuity through the single vision glasses. This improvement remained stable at the six month follow up visit. Other measurements of literacy (including the Dolch sight words test) showed a statistically significant improvement after bifocal wear.

It is clear from this study that bifocals are a viable treatment option for children with DS who have inaccurate accommodation. Another clinically significant benefit for children with DS who have poor accommodation is that spectacle lens correction will remove the blur associated with low hyperopia, and will decrease the likelihood of amblyopia. While children without DS may gain no benefit from the correction of small amounts of hyperopia, this should not be assumed to be the same for children with DS.

Strabismus

Differences in binocularity in DS

Strabismus is seen more frequently in children with DS having a prevalence of 19%⁵² to 34%³⁹ (see table 4).

Table 4 The frequency with which the different types of strabismus are seen when strabismus is present, compiled from references ^{32, 39, 52, 53}

Esotropia	84-90%
	Alternating 70%
	Constant 57%
	Intermittent 23%
	Monocular 30%
	Strabismus Eliminated with Glasses 19%
Exotropia	8-10%
Vertical Deviations	2-8%

Accommodative strabismus is expected to be more common in a population with a high prevalence of hyperopia. The results of Haugen et al show that the frequency of hyperopia was greater in those with

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strabismus compared to those without strabismus – 46% and 13% respectively.⁵³ The importance of uncorrected hyperopia as a cause of accommodative strabismus is highlighted by the finding that 22% of the children who had less than 2DS of hyperopia had strabismus while 75% of those who had more than 4DS of hyperopia were strabismic. The results of Haugen et al show that when esotropia is present it is more likely to be alternating (70%) than unilateral (30%). Da Cunha et al³⁹ found that non accommodative and accommodative esotropia were equally common. Da Cunha et al also attributed the vertical deviations in their population to congenital fourth nerve palsy (3 of 4 cases) and double elevator palsy (1 of 4 cases).³⁹

Changes in binocularity with age

The longitudinal study of Haugen et al⁵³ followed sixty children with DS for a minimum of two years. They found that only two children had strabismus in infancy. Both were detected at 11 months of age and the strabismus was small angle esotropia. However by the end of the study 25 out of 60 children (42%) were found to have strabismus. The mean age when the strabismus was detected was 54 ± 36 months (4.5 \pm 3 years). This late onset of the strabismus may be linked to the potential failure of emmetropisation in DS and accommodative esotropia in those with uncorrected hyperopia and accurate accommodation. In children without DS, the age of onset of accommodative esotropia is typically at 2-3 years.⁵⁴ Da Cunha et al³⁹ found the average age of onset of accommodative esotropia in DS to be 4.5 years of age. This later age of onset may be attributed to the developmental delay of these children and to the increased incidence of high refractive error which changes with time. The high incidence of strabismus goes hand in hand with the development of amblyopia.

Amblyopia and Strabismus

Ljubic et al⁸ reported the frequency of amblyopia, (defined as a difference in visual acuity between the eyes of two lines on a Snellen chart), to be 17% in a group of children and young adults with DS between 1-34 years of age. This demonstrates that children with DS need regular eye examinations so that these deviations can be detected early and managed appropriately. If the refractive error is found and corrected early in the child's development and corrected this will enable the child to attain the best visual acuity

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possible. It will also stimulate cortical development and prevent amblyopia. It may also prevent the formation of accommodative strabismus.

Aetiology

One would expect a high prevalence of hyperopia to go hand in hand with refractive and accommodative esotropia, which if refraction was not fully corrected, could explain the high prevalence of eso deviations. However, if accommodation is reduced then this cause is less likely. In addition Ljubic et al⁸ found that eso deviations were more associated with hyperopia (40% of those with DS and esotropia were hyperopic), but were also quite common in myopia (28% of those with DS and esotropia were myopic). A high prevalence of eso deviations in a population also with a high prevalence of insufficient accommodation may be explained by the accommodation-vergence system. Perhaps the AC/A ratio will increase as the amplitude of accommodation is reduced due to an effort to make reading material clear. Consequently, additions to treat convergence excess may be more relevant for this segment of the population. This theory requires further investigation.

Management

The conventional approach to management of hyperopia and esotropia (full correction of the refractive error, assistance with a near addition if necessary) is appropriate for children with DS.

However it is particularly important that alignment and refractive error problems are detected early so that latent deviations are managed before adverse sequelae develop. This is especially important in the DS population as these deviations are more commonly encountered.

Muscarinic Antagonists

Cyclopentolate is used commonly by optometrists as part of the refraction procedure. Atropine is used as an alternative to patching in the treatment of amblyopia and also for myopia control in children. There are adverse systemic effects of muscarinic antagonists which include "ataxia, incoherent speech, restlessness, hallucinations, hyperactivity, seizures, disorientation to time and place, and a failure to recognise

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people.”⁵⁵ Harris and Goodman⁵⁶ have shown that individuals with DS have a greater increase in heart rate to higher doses of intravenous atropine than controls but more recent evidence^{57, 58} has enabled the conclusion that the quantity of drug reaching the systemic circulation from eye drops is such that the reports of increased susceptibility to the toxic effects of atropine eye drops in DS are unfounded.

Atropine is a far more potent anticholinergic than cyclopentolate. Atropine, as a non-selective muscarinic antagonist, binds to all five subtypes of muscarinic receptors on the iris sphincter and ciliary body.

Cyclopentolate is a selective muscarinic antagonist that binds to fewer receptors than atropine and has a shorter duration of action and a better safety profile.^{59, 60} While a number of studies report conducting cycloplegic refractions on children with DS^{13, 29, 32, 61} only two^{13, 61} provide information about adverse reactions. Neither of these studies reported adverse reactions for a combined sample size of 50 and an age range of 4 months to 19 years.

For safety, the minimum dosage needed for children with DS should be used, and caution (including punctal occlusion to minimise systemic absorption) should be observed with cyclopentolate.

Cataracts

Creavin et al⁶² reported the results of eighteen studies which assessed cataract. In eight of these the prevalence was 5% or less, in eight the prevalence was between 6% and 15% while two studies found the prevalence to be 20% and 37%. A Danish study⁶³ estimated the prevalence of cataract in DS at birth to be 1.4% compared to that in the general population of 0.06%. Cataracts diagnosed later in childhood are probably less likely to be visually significant. 71% of cataracts diagnosed after 12 years of age were Cerulean or blue dot in origin. Cerulean cataract has been linked to Chromosome 22 but not Chromosome 21.⁶⁴ If not detected by paediatricians and treated early, congenital cataracts are likely to cause amblyopia. Visually significant cataracts can develop before age eighteen and it is the role of optometrists to detect these and to refer appropriately.

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Brushfield Spots

Brushfield spots are focal areas of iris stromal connective tissue hyperplasia surrounded by relative hypoplasia. They appear as speckled spots and are found in 0%^{65, 66} - 52%³⁹ of children with DS. They are of no functional significance, are more common in those with light irides and may become less visible with age if iris colour turns from blue to brown.⁶⁷ The lack of Brushfield spots in dark irides probably explains why these were not found in studies of Italian and Malaysian children with DS.^{65, 66}

Blepharitis

Creavin et al⁶² reviewed eleven studies which provided data for the prevalence of blepharitis. In six of the studies the prevalence was 10% or less, three found the prevalence to be 15-20% and two found the prevalence to be 15-30%. Blepharitis can cause itch which may induce eye rubbing. This may have significance in that eye rubbing has a role in the development of keratoconus, which is also found to be more prevalent in DS.

Conclusions

1. Down syndrome (DS) is the most common of the human chromosome abnormalities. Optometrists should have an excellent understanding of how DS affects vision so that suitable assessment techniques can be used and appropriate management can be provided.
2. When examining a child with DS, a target of appropriate design and size should be used which is tailored to the child's ability.
3. Refractive errors often increase with age rather than approach emmetropia as is usually found in the general population. Therefore review appointments should be scheduled more frequently. The unpredictability of refractive error development should be taken into account when deciding whether to correct the child's refractive error. There is currently no explanation for why this occurs in DS.
4. Oblique astigmatism is more common in DS. This is likely to change in axis and magnitude over time due to the obliquity of the child's palpebral fissures. Review appointments should be more frequent.

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5. Strabismus, especially eso deviations are common in DS. Accommodative esotropia is reported to have a later onset of 4.5 years in children with DS. This is important information for advice to the parents and teachers of these children.

6. Visual acuity may be decreased in children in DS. This is mostly attributed to optics of the eye and the presence of uncorrected refractive error, and partially to a cortical deficit. Poor acuity and reduced contrast sensitivity results are not explained by a lack of visual attention when appropriate tests of visual performance are used. All children with reduced acuity should have a thorough examination to rule out ocular pathology.

7. Accommodation should be measured using an objective technique and bifocals considered if accommodation is found to be deficient.

8. Cataract, blepharitis and keratoconus are more common in DS and should be checked for at eye examinations.

9. With an understanding of some of the ocular differences in children with DS, optometrists can be better equipped to assess and manage these patients.

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