The functional impact of amblyopia

Amblyopia is second only to uncorrected refractive error as the most common cause of poor vision in children and young people. With prevalence of approximately three per cent of the population, amblyopia has significant costs to both the individual and community in terms of screening and treatment. While much has been reported about the visual characteristics of amblyopia, the natural history of the condition and appropriate detection and treatment strategies, the functional disadvantage of amblyopia has only more recently been specifically explored, particularly in the childhood population in whom amblyopia is most often diagnosed and treated. Indeed, the ethical basis for detecting and treating amblyopia or its risk factors without evidence of disability was directly questioned in Snowden and Stewart-Brown’s 1997 review of the literature regarding effectiveness of preschool vision screening. Snowden and Stewart-Brown noted that the literature at that time provided a ‘reasonable basis for generating plausible hypotheses about the ways in which the target conditions might disable people, but is insufficient to draw any firm conclusions about their impact on quality of life’.

The intervening two decades has seen revived interest in determining the extent to which amblyopia affects the ability to carry out everyday tasks, including studies of the relationship between the visual deficits that accompany amblyopia and everyday task performance. Crucially, there are recent studies that demonstrate functional performance improves with amblyopia treatment.

The usual risk factors for amblyopia are strabismus (which disrupts binocular fusion), refractive error (particularly anisometropic hyperopia), or more rarely an obstruction in the optical pathway that reduces retinal image quality (such as congenital cataract). Rather than clinically apparent ocular or visual pathway pathology underlying the reduced vision, the predisposing conditions disrupt the normal postnatal development of the visual system. An array of monocular and binocular vision anomalies have been identified in amblyopia which include decrements in high contrast visual acuity, contrast sensitivity, positional certainty and depth perception, with amblyopia aetiology influencing the pattern of visual performance loss. However, the relative contributions that the documented vision anomalies inherent in amblyopia contribute to various functional disabilities have yet to be fully determined.

Controversially, conclusions regarding the extent of disability that can be attributed to amblyopia are varied, with patient-reported outcome measure qualitative studies suggesting areas of difficulty that have not been quantified in studies of functional performance. Indeed, population-based studies and reviews of educational, health and social outcomes, have failed to identify any ‘real life’ functional impact of the visual deficits associated with amblyopia, and emphasise the need for further research on what it means to be amblyopic. In contrast, there are now a number of studies that report relative performance of amblyopic observers under habitual supra-threshold binocular viewing conditions. This emerging body of evidence describes deficits in functional performance that may occur with amblyopia or its visual consequence, particularly in the areas of motor skills proficiency and reading. Randomised controlled treatment trials and reviews of patients who have not been compliant with treatment have established that intervention is required for amblyopic vision deficits to recover, and recently we have shown that successful treatment improves fine motor skills performance.

Determining the long-term impact of amblyopia, the extent of functional disability that can be attributed to the condition...
and evidence that intervention improves function, is necessary to support programs which aim to identify and treat amblyopia. In this review the functional disadvantage of amblyopia is discussed from a number of perspectives, commencing with a brief summary of impact of amblyopia on monocular and binocular vision, impact on whole-of-person functioning and occupational choices. Particular emphasis is given to the contemporary studies that have explored visually directed fine motor skills and reading performance of children with amblyopia, strabismus or both.

**Visual deficits in amblyopia**

Amblyopia principally affects one eye; nonetheless, the non-amblyopic eye often has an array of small but measurable deficits of spatial, positional and motion sensitivity. Clinically, high contrast recognition visual acuity is the predominant measure that leads to a diagnosis of amblyopia, based on two or more lines difference in visual acuity measured between eyes. The amblyopic eye may also have poorer grating acuity, poorer vernier acuity, poorer contrast detection thresholds and altered contrast sensitivity function, the pattern of which varies between aetiological groups. In addition to deficits determined at threshold, amblyopic vision has disturbance at supra-threshold levels, including perceived spatial distortion, such as misperception of orientation and positional uncertainty.

Binocular vision perception is usually altered in amblyopia with suppression or abnormal retinal correspondence leading to degraded sensory fusion and poor or absent stereopsis. Most patients with a history of early-onset strabismus have little or no clinically measurable bi-foveal sensory fusion or stereovision, even if visual acuity has improved after treatment and no longer meets the clinical amblyopia criteria of a two-line difference in visual acuity between eyes. In contrast, residual stereovision or binocular motion integration is often present in anisometropic amblyopia. Stereovision improves with amblyopia treatment; however, rarely recovers to a normal level even when visual acuity completely recovers.

Under habitual binocular viewing conditions, threshold visual acuity is generally equal to that of the dominant eye, which can be within the normal range of acuity for age. However, reduced or absent depth perception is a liability present during binocular viewing conditions and may represent the main visual function disadvantage between patients with amblyopia and those without when performing everyday tasks. Many of the poor functional performance tasks that have been assessed in amblyopic groups are not visual acuity limited but may relate to extent of binocular function loss.

When tested under monocular viewing conditions, the amblyopic eye is reported to have reduced amplitude and less accurate accommodation than the fellow eye and when compared with control subjects, particularly at higher accommodative demand fixation distance; however, the inter-ocular difference in accommodative response is minimal (<0.10 D) under binocular viewing.

Oculomotor deficits including inaccurate or unsteady fixation, delayed and more variable initiation of saccades, and inaccurate tracking pursuits have been recorded in amblyopic subjects. While amblyopic eyes show poorer fixation stability than control eyes during both monocular and binocular viewing, fellow eyes have fixation stability comparable to that of controls, both when fixating or under binocular viewing. However, the initiation of tracking pursuits is delayed and saccadic latency of the non-amblyopic eye can be less accurate than in age-matched controls.

**Impact on whole-of-person functioning and occupational choices**

The impact of amblyopia and potential for reduced quality of life has been reported from a population perspective. The likelihood of visual disability due to loss of visual function of the non-amblyopic eye can be calculated and is an argument for amblyopia treatment that aims to maximise visual potential in the affected eye. The lifetime risk of bilateral vision impairment is nearly double that for amblyopes than for controls, being as high as 18 per cent for those with amblyopia, compared with 10 per cent in non-amblyopes, while the projected lifetime risk of visual impairment following loss of the better eye is 1.2 per cent. Two out of three amblyopes who have lost vision in their better eye cannot continue in paid employment. Chua and Mitchell examined the consequences of amblyopia for education, occupation and long-term vision loss and reported that amblyopia did not affect lifetime occupational class, although relatively few amblyopes obtained university degrees. People with a history of amblyopia are reported to feel it has affected their school and career choices; however, birth cohort studies report that amblyopia does not significantly impact educational, health or social outcomes. Children with amblyopia do as well as their peers in age-appropriate tests of mathematics, reading comprehension, and perceptual and motor skills, and are generally not more likely to have significant behavioural problems or maladjustment at home or school than those without amblyopia.

Adult amblyopes with a moderate to severe visual acuity deficit (6/18 or worse) were more likely to report having had a road accident when they were the driver that resulted in injury requiring hospital care. However, the impact of amblyopia and the importance of stereopsis to driving remain unclear. Reports of the benefit of normal binocular vision on driving safety are inconsistent in findings, with some studies finding better driving outcomes among motorists with normal binocularity while others find little correlation. When navigating a short slalom course, stereo-deficient strabismic drivers were worse than controls; however, they were not worse at stopping in front of an obstacle, reversing into a parking space, or estimating the relative positions of two cars.

Specific studies of driving performance of amblyopic motorists are needed to further inform the debate regarding this potential functional consequence. Potentially, amblyopes who have lived with altered visual perception most of their life will perform better than drivers who lose vision in one eye later in life. Therefore, attributing the findings of older monocular drivers to amblyopes may not be justified.

Patients with amblyopia can be excluded from a wide range of jobs, which increases with the severity of the amblyopia. Poor visual acuity in one eye may prevent qualification for a commercial driver’s licence and can be below the minimum visual standard required for some career choices. In addition, a demonstration of a moderate degree of stereopsis (that is, at least 80 arcseconds) has been suggested as a binocular vision standard on the premise that
ability to appreciate the depth of one object relative to another is required for efficient and safe job performance. While vision standards may be amended over time, they can preclude vocational choices for applicants with amblyopia.

Questionnaire-based patient-reported outcome measures have been utilised to determine quality of life impact of amblyopia in both paediatric and adult populations. However, many patient-reported outcome measures instruments are directed to cosmetically obvious strabismus and its social impact and are not specific to amblyopia per se. In addition, most amblyopia-specific questionnaires have measured health-related quality of life during the treatment phase when the vision of the better eye is absent or degraded, and fail to address function under habitual binocular viewing conditions.

While the use of patient-reported outcomes, such as health-related quality of life questionnaires, can be useful in determining the impact a condition has on an individual, most patient-reported outcome measures instruments have been developed for application in Western English-speaking countries and may not fully determine the quality of life impact for patients of other cultures whose activities and responses may differ.

Impact on reading proficiency
Reading is recognised as an important vision-dependent ability that contributes to an individual’s quality of life. A growing number of studies report reduced reading proficiency in children with amblyopia compared to those with normal vision development; however, prevalence of specific reading disability among amblyopes is similar to that of the general population. In addition to reliance on resolution of font, the reading process requires a coordinated execution of saccadic eye movements that is described by several features, namely fixations, regressions, return-sweep saccades, span of recognition, fixation duration and reading rate. Adults with strabismic amblyopia are shown to read more slowly than controls under both monocular and binocular viewing conditions, with increased number of regressive saccades and prolonged fixations duration contributing to the decrease in reading speed. When tested under binocular viewing conditions, children with micro-strabismic amblyopia had a small but significant reduction in maximum reading speed (173 ± 44 words/minute) than controls (200 ± 11 words/minute). Better binocular reading speed in the amblyopic group was associated with more central and steady fixation and better sensory binocular function, but did not relate to age, visual acuity, accommodative impairment, strabismic angle or refractive error.

Decreased reading speed while silently reading an age-appropriate booklet of paragraphs under normal binocular viewing conditions was related to amblyopia, but not strabismus. Children with amblyopia read more slowly (148 ± 52 words/minute) and make more saccades than both children who were no longer amblyopic after treatment of strabismus (198 ± 71 words/minute) and normal controls (204 ± 62 words/minute). Within the amblyopic group, reading rate did not associate with the impact of amblyopia or severity of visual acuity deficit.

Abnormal eye movement control and poor accuracy and stability of fixation have been suggested as direct causes of the poor reading skills. Accuracy and stability of fixation and saccades is poorer in amblyopic eyes and binocular coordination of saccades is impaired in strabismic amblyopes, particularly those with large angle strabismus.

The developmental eye movement (DEM) test determines the speed with which a series of numbers can be recognised and verbalised with accuracy and is purported to provide an indirect evaluation of saccadic eye movements. However, no difference was found between children with and without amblyopia on DEM test outcome speed and accuracy measures and the prevalence of clinically unacceptable results did not differ between groups. Further, outcome measures of the DEM test did not significantly correlate with measures of acuity or level of binocularity or history of strabismus. A characteristic of amblyopic acuity is its susceptibility to the crowding phenomenon, where a letter that is easily recognised on its own becomes unrecognisable if surrounded by other letters or flanking bars. Crowding rather than acuity, has been shown to limit monocular reading in both amblyopic and normal observers, both in central and peripheral vision. Unlike reading, performance on the DEM test is unlikely influenced by crowding because the test targets consist of 3 mm tall, high-contrast single digits (approximately N10) with 5 mm between rows of numbers and spacing of 10–25 mm between numbers. Further, crowding would not be anticipated to contribute to reduced resolution during binocular viewing conditions.

Collectively, reading proficiency studies demonstrate a reduced reading rate in amblyopia when tested under habitual binocular conditions. However, the relative contribution of spatial vision deficit, oculomotor control and accommodation accuracy and stability to this crucial real-world skill has not been conclusively determined. The impact of reported accommodation response errors on reading proficiency has not been specifically explored, nor has the benefit of treatment to reading rate been determined.

Impact on fine motor skills proficiency
There is growing evidence that children with amblyopia have worse motor skills than children with normal vision. These studies commonly describe the detrimental effect of amblyopia on real-world visuomotor skills that are important for everyday activities such as reaching and grasping, drawing, writing and manual dexterity tasks. Larger fine motor skill deficits have been associated with worse amblyopic eye visual acuity and stereopsis. Sugesting that motor deficiencies may be secondary to the visual impairments resulting from amblyopia.

Non-strabismic, pre-school children with reduced acuity in one eye (6/9 to 6/60; n = 28) showed reduced performance on a fine visual-motor control bead threading task which related to stereoaucity, independent of visual acuity. However, ability on other items in the battery (measures of visual-motor integration, visual spatial processing, visual attention and gross visual-motor skills) was similar to that of age-matched controls. In an older cohort (age 12–28 years) better stereoacuity, sensory fusion and motor fusion range was associated with superior performance on motor skills tasks that involved moving pegs on a pegboard, threading beads on a string and pouring water.

A small number of studies have specifically compared skills between children with and without amblyopia. Children with anisometropic amblyopia aged seven to
13 years were worse than control children at transferring answers on multiple choice answer sheets and on manual dexterity sub-tests of Movement Assessment Battery for Children 2; however, the scores did not associate with visual acuity or stereoaucity. When older amblyopic children (aged 8.2 ± 1.7 years) from a range of causes were assessed on standardised developmental tests of fine motor skills under habitual binocular vision viewing conditions, their performance was poorer than that of age-matched controls, particularly in those with a history of strabismus. The deficits in performance of the amblyopia group are more marked in the timed manual dexterity tasks than visual motor copying activities: the amblyopes scored on average 3.70 standard points lower than controls on the manual dexterity item, while the difference between amblyopes and controls was 1.73 standard points for the visual motor copying item. Overall, a global reduction in performance of the group with amblyopia was observed, rather than a few individuals showing large deficits. Further, the proportion of children whose score was clinically rated ‘below average’ was greater in the group with amblyopia (17 per cent) than without (three per cent).

Significant differences in scores were also apparent between amblyopia subgroups, in that not all of the aetiology groups displayed a deficit in fine motor skills. Further, when a multiple regression analysis was employed that accounted for intercorrelation between possible explanatory factors, such as extent of visual acuity or binocular function loss or aetiology, a history of strabismus was the predominant influencing factor on fine motor skills score. This suggested that the cause of amblyopia or the neurological mis-wiring that occurs in the different aetiology groups, rather than the extent of the clinical visual deficit, determined the impact of amblyopia on fine motor skill development. Whether this is related to spatially distorted vision that is particularly marked in strabismic amblyopia, or reflective of the extent of neural changes that occur in different amblyopia types remains speculative.

The kinematic parameters defining reaching and grasping required in eye-hand coordination skills have been examined in both adults and children with amblyopia. Adults with amblyopia show a range of deficits in their approach to an object and when closing and applying grasp, under both binocular and non-dominant eye viewing conditions. Prolonged execution times and more errors were found in the amblyopic group than the control, which co-varied with depth of amblyopia, but not aetiology. Similarly, children with amblyopia were slower and made more errors than those with normal vision, particularly those amblyopic children with poorest binocularity, regardless of severity or cause of their amblyopia.

The planning and execution of visually guided saccadic eye movements and reach to touch hand movements is disrupted in amblyopia. While the latency and precision of reach to touch movement varies with severity of visual acuity deficit and reach strategy relates to stereopsis, more than 50 per cent of the variance in performance was not explained by these clinical measures. Strategies employed by amblyopic children for precision to reach and grasp objects change with age, with speed and accuracy of movements related to severity of visual acuity and stereoaucity decrement.

While not a specific treatment intervention study, motor skills performance was compared between children with amblyopia, non-amblyopic children previously treated for strabismus and control children with normal vision development. Amblyopic children had poorer manual dexterity scores than both the treated strabismus and normal controls, which did not relate to amblyopia type or severity or stereoaucity, while the treated strabismic group and normal control group had similar scores. Eleven (38 per cent) amblyopic, seven (32 per cent) non-amblyopic strabismic, and three (14 per cent) control children were at-risk or impaired on total motor ability (≤ 15th percentile). Collectively, these studies provide insight to the detrimental effect of amblyopia and/or strabismus on visuo-motor development, execution of practical visuo-motor tasks and the kinematics of movement underpinning performance. However, reduction in visual acuity, reduced stereopsis, positional uncertainty and aetiology are highly related, making it difficult to disentangle the relative contributions of each to motor control, particularly in smaller sample studies. What requires more evidence is whether these skills are ameliorated by amblyopia treatment. Future amblyopia treatment studies could consider inclusion of measures of manual dexterity as an outcome parameter in addition to testing for change in acuity or binocular function.

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**TREATMENT**

Do motor skills improve with treatment?

Over the last 20 years there have been a number of reports on amblyopia treatments that aim to improve visual acuity and restore binocular function in adults. Levi et al. collated data from published studies that report change in stereopsis following activities aimed to treat amblyopia. Across the various treatment methods, including patching, perceptual learning, dichoptic activities and direct stereo training, more than a quarter of amblyopes with no prior measurable stereopsis had measurable stereopsis post-treatment. More than half of anisometropic and about a quarter of strabismic amblyopes showed at least a two-level improvement on a test (for example, from 200 arcseconds to 100 arcseconds on the Randot Circles) and stereoaucity of 160 arcseconds or better. Collectively, the studies demonstrate quite clearly that, even beyond the generally accepted critical period, recovery of at least some degree of stereopsis is possible.

A more limited number of studies indicate that treatment of amblyopia or strabismus will impart improved motor skills outcomes for patients; however, the vast majority of amblyopia treatment studies to date have not specifically included motor function as an outcome measure. Delayed neuro-developmental sensorimotor and gross motor skills reported in infants with strabismus are found to rapidly recover post-strabismus surgery, and more recently, improved reach to grasp performance following occlusion therapy was reported in a small pilot group (n = 4) that appears related to improved stereovision.

We have been the first to specifically assess whether the visuo-motor skills deficits that occur with amblyopia improve following amblyopia treatment. Five weeks of home-based binocular treatment improved performance on an aged-standardised battery of timed manual dexterity tasks in children with residual amblyopia, and change in performance score was above the test–retest variability that might arise with repeated measurement. The measured improvement was sustained for a three month period post-
training (Figure 1). The amblyopic children with better baseline acuity and binocular function showed greatest improvement in motor skills score, which in this sample was anisometropic rather than strabismic amblyopes. Whether the improvements found were specific to binocular treatment employed in the study or whether they would also occur with conventional occlusion amblyopia treatment was not determined. Additional work is required to further examine how treatment may ameliorate performance deficits reported in amblyopia. Inclusion of visuo-motor control as an outcome measure in future amblyopia treatment trials may provide an indication of the treatment effect on a crucial, real-world skill required for optimal development.

**Impact on higher order processing**

Neurophysiological evidence indicates dysfunction in amblyopes in both primary

Figure 1. Changes in fine motor skills in amblyopia and comparison groups. (FMS = age-standardised score attained on Upper Limb Speed and Dexterity test battery of Bruininks-Oseretsky Test of Motor Proficiency. Higher score indicates better performance). A: Filled bars show amblyopia group mean FMS before (baseline), directly after (post-five weeks treatment) and three months after (follow up) treatment. Open bars show mean data for the comparison group with normal vision at baseline and five weeks later (post-five weeks). Error bars show ±1 SEM. B: Individual data for the amblyopia group. The unity line light dashed lines either side of the unity line indicate the 95 per cent CI for change (test–retest variability) from the comparison group. Data points falling above the upper dashed line represent a change in FMS score that exceeded test–retest variability. C: Individual test–retest data for the comparison group with normal vision. Data reported from Webber et al.6
(V1) and secondary (V2) visual areas, regions within the parieto-occipital cortex and the ventral temporal cortex.\textsuperscript{82} The most profound and consistent changes in the visual pathways are at the striate cortex;\textsuperscript{6} however, amblyopia is also believed to impact on the extra-striate pathways, predominantly those which process motion information,\textsuperscript{83} although the extent of these changes is less well known. Reduced responses are evident at the level of the lateral geniculate nucleus, with the relative responses to chromatic versus achromatic stimuli suggesting loss of parvo-cellular function.\textsuperscript{84}

Psychophysical studies support the hypothesis that abnormalities in area V1 are amplified in V2 and possibly beyond. Losses are evident in second-order detection, global form and motion integration, symmetry detection and counting with evidence for these findings in human studies reviewed by Levi.\textsuperscript{19} 19

The downstream impact of amblyopia on local and global and higher order processes required during visuo-motor activities for the initiation and execution of eye movements, and planning and execution of reaching and grasping hand movements additionally requires consideration.\textsuperscript{79} Adults with amblyopia show deficits in response time for complex visual decisions, suggesting impaired higher-order perceptual decision making.\textsuperscript{85} Children with both strabismic and anisometropic amblyopia have shown deficits in attentive tracking of single and multiple objects with both amblyopic and fellow eyes, suggesting impaired functioning of the parietal cortex.\textsuperscript{86}

Visual attention, processing speeds and visuo-cognitive search ability were recently assessed in children with and without amblyopia.\textsuperscript{87} The children completed computer-based assessment of visual attention for increasingly complex tasks\textsuperscript{88} that require detection, identification and localization of briefly presented central and peripheral targets as well as an assessment of visual search and scanning, psychomotor speed and executive function. Children with amblyopia exhibited reduced performance on visual attention, visual search and scanning tasks, compared to age-matched controls.\textsuperscript{87} Future work should explore the implications of these executive function impairments on fine motor skills and reading, and whether these functions improve following treatment for amblyopia.

CONCLUSIONS

For many years, early childhood vision screening programs have aimed to provide a safety net by identifying children with risk factors for amblyopia while they are still within the critical period of treatment efficacy (traditionally believed to be up to about eight years of age). To date, the two main objectives of early detection and treatment of amblyopia or its predisposing conditions are, first, to improve acuity in the affected eye and improving potential for binocular vision, and second, to reduce the risk of visual impairment later in life if the non-amblyopic eye loses its function through disease or injury.

Debate continues regarding the benefits of community-funded early childhood vision screening programs, with the cost-effectiveness of screening found to be dependent on the long-term utility effects of loss of vision in one eye.\textsuperscript{12} The benefit of an improvement in visual ability in the amblyopic eye can also be quantified by improved quality of life scores and indicate positive cost-analysis of treatment.\textsuperscript{89,90}

While the balance between debility attributable to the condition versus the treatment has not been established, the potential disability of incapacitating vision loss later in life, due to loss of visual function of the non-amblyopic eye, can be calculated and is an argument for treatment to maximise visual potential in each eye.\textsuperscript{37}

In addition to qualitative evidence, review of the literature suggests significant impact of amblyopia on visually directed skills and most of these studies attempt to correlate performance on fine motor skills with a deficit in visual acuity or reduced stereopsis.\textsuperscript{21,69,70} However, because many of the motor tasks are not scored at threshold acuity level, they are not limited by the acuity deficit that defines the amblyopia, particularly under binocular vision conditions. Moreover, the tasks also require higher order processing to drive the visual input to a motor output. The downstream impact of amblyopia on processing beyond the primary visual cortex has not been fully determined but is likely to be an influencing factor.

The relative contributions of the array of visual consequence of amblyopia (reduced acuity, impaired or absent stereopsis, spatial distortions or positional uncertainty) to performance on visually directed manual dexterity, reading efficiency and under supra-threshold binocular viewing conditions remains to be fully ascertained. While there has been a number of studies that now report the functional liability associated with amblyopia that may impact on everyday activities and may limit career choices, we await the outcome of further studies to confirm that successful treatment may remediate the functional disabilities of amblyopia.

REFERENCES

The functional impact of amblyopia

Webber


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