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Age- and stereovision-dependent eye-hand coordination deficits in children with amblyopia and abnormal binocularity

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Purpose: To examine factors contributing to eye-hand coordination deficits in children with amblyopia and impaired stereovision.

Methods: Participants were 55 anisometric or strabismic children aged 5.0-9.25 years with different degrees of amblyopia and abnormal binocularity along with 28 age-matched visually-normal controls. Pilot data were obtained from 4 additional patients studied longitudinally at different treatment stages. Movements of the preferred hand were recorded using a 3D motion-capture system while subjects reached-to-precision grasp objects (2 sizes, 3 locations) under binocular, dominant eye and amblyopic/non-sighting eye conditions. Kinematic and 'error' performance measures were quantified and compared by viewing condition and subject group using ANOVA, stepwise regression and correlation analyses.

Results: Movements of the younger (age 5-6) amblyopes (n=30) were much slower, particularly in the final approach to the objects, and contained more spatial errors in reaching (~x1.25-1.75) and grasping (~x1.75-2.25) under all three views ($p < 0.05$) than their age-matched controls (n=13). Amblyopia severity was the main contributor to their slower movements with absent stereovision a secondary factor and the unique determinant of their increased error-rates. Older (age 7-9) amblyopes (n=25) spent longer contacting the objects before lifting them ($p = 0.015$) compared to their matched controls (n=15), with absence of stereovision still solely related to increases in reach and grasp errors, although these occurred less frequently than in younger patients. Pilot prospective data supported these findings by showing positive treatment-related associations between improved stereovision and reach-to-grasp performance.

Conclusions: Strategies that children with amblyopia and abnormal binocularity use for reach-to-precision grasping change with age, from emphasis on visual feedback during the 'in-flight' approach at ages 5-6 to more reliance on tactile/kinesthetic feedback from object contact at ages 7-9. Recovery of binocularity, however, confers increasing benefits for eye-hand coordination speed and accuracy with age, and is a better predictor of these fundamental performance measures than the degree of visual acuity loss.

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Introduction

Binocular vision provides a number of well-established perceptual advantages over monocular viewing, most notably in enhancing distance and depth discrimination for solid objects and surfaces (stereopsis) in near-space. This stereoscopic information also affords significant advantages for evaluating the visual scene during the planning of goal-directed movements of the limbs in immediate 3D space, such as the hand for grasping objects¹ and the feet for stepping down or over obstacles^{2,3}. Indeed, even human infants just weeks after the normal emergence of binocular distance and depth sensitivity (between 3-6 months of age) are better able to judge whether objects are within their reach and to execute movements towards them using two eyes than with one eye covered⁴⁻⁶. It is also clear that stereovision confers major advantages for providing the fast and reliable feedback required for 'on-line' movement guidance and adjustment of the grasping hand relative to the goal object^{1,7-11}, although use of such feedback for improving performance does not appear to be prioritized until later in normal development, at about ages 7-8 years¹²⁻¹⁴.

Unfortunately children with unequal refractive errors between the two eyes (anisometropia) or a squint (strabismus) between birth and these later ages commonly have defective stereovision¹⁵ and often develop amblyopia. This disorder is associated with abnormal responses to the affected (amblyopic) eye in the visual cortex¹⁶, with reductions in its visual acuity (VA) accompanied by 'higher level' deficits in spatial, object and motion perception¹⁵⁻¹⁹ along with impaired performance on a variety of visually-guided real-world 3D tasks²⁰. For example, we²¹ quantified reach-to-precision grasp actions in a sample of 21 children aged 4-8 years with amblyopia of either subtype and found that their movements were slow, 'uncertain' and poorly coordinated under natural viewing conditions (i.e., with both eyes open) and when using just their amblyopic eye – and even their better eye alone – compared to the equivalent binocular and monocular performance of age-matched normally-sighted peers. There were also indications that the clumsiest performers across all views were those lacking measurable stereoacuity, suggesting that some degree of binocularity is needed for the acquisition of skilled eye-hand coordination abilities in childhood.

Importantly some of these eye-hand coordination problems during habitual binocular – although not dominant eye – viewing also apply to adults with persistent amblyopia²² and even to adults whose VA deficits had previously been 'cured' by childhood amblyopia treatment, but who remain stereo-impaired²³. This latter situation further suggests that loss of

binocularity cannot be compensated for by more efficient use of numerous alternative, monocular cues to object distance and/or depth, even with long term practice. We did, however, obtain evidence²³ of a strategic change underlying a partial grasping adaptation, whereby adults with stereovision losses placed greater reliance on tactile/kinesthetic (i.e., non-visual) feedback derived from initial digit-object contact to modify their grip and ensure its stability.

These findings have significant implications for current amblyopia therapies, which primarily aim to reverse the VA loss in the affected eye, first by a period of optical correction via spectacle wear (termed 'refractive adaptation'), usually followed by daily periods of patching (occlusion) of the dominant eye. Most children who comply with these treatments achieve significant gains in VA²⁴⁻²⁷, and in those with anisometropia or small-angle strabismus stereoacuity may also improve^{28,29}. However, if binocular recovery really is the key to reversing the real-world visuomotor deficits in amblyopia, a greater focus on reinstating the stereovision – rather than visual acuity – loss would be warranted, as we²⁰⁻²³ and others have recently suggested^{16,30-33}.

Here we extend our preliminary observations by examining eye-hand coordination abilities in a much larger cross-sectional group of 55 children with varying degrees of VA and stereoacuity loss at different stages of amblyopia therapy, and in another 4 children studied prospectively during their routine clinical management. The aims were to determine whether this more extensive analysis would support our initial conclusions regarding the importance of binocular visual recovery for enhancing reaching and grasping skills in these patients, distinct from other potential contributory factors such as their age, severity of amblyopia or its treatment stage. For example, we previously confirmed²¹ that normally-sighted children aged 5-6 generally adopt a feedforward reach-to-grasp strategy, in which vision is used mainly for movement planning, with visual feedback used to reduce spatial errors (i.e., inaccuracies) in movement execution employed only at later ages. But any such analogous use of on-line control or of adaptive strategies by older children with amblyopia that may have improved their performance independently of their visual deficits – an important issue from both biological and clinical management perspectives – could not be determined, as only a few (5/21) of the patients tested were aged 7 years or older.

MATERIALS AND METHODS

Cross-sectional data were obtained from 83 children aged 5.0-9.25 years, of whom 55 were either undergoing (n=24) or had recently completed (n=31) treatment for amblyopia (with varying degrees of success) and 28 were normally-sighted controls. All subjects had standard clinical vision tests conducted by one of the authors just before their eye-hand coordination abilities were assessed. For the patients, this was always on the day of a routine clinical appointment and included evaluations of logMAR distance VA in each eye, of stereoacuity and, in those deemed necessary, of suppression (Bagolini lenses, followed by Worth 4-dot lights, when this was inconclusive). The initial stereo test was for 'gross' (3000 arc secs) stereopsis using the Titmus Fly. Patients passing the Fly were examined further with the Titmus circles and then, in most cases, the Frisby test. As the results of these tests were well correlated ($R^2=0.89$, $p<0.001$; $n=19$), the lowest (best) score was recorded as the stereo-threshold. Solid stereograms were used because they are more akin to real-world 3D stimuli (which also contain monocular depth cues) and are easier for children to understand (and, hence, to administer), than random-dot displays. When not directly tested, other patient data, for example, on refractive error, suppression, cover test, ocular motility, convergence and prism fusion ranges, were obtained from their earlier clinical appointment record.

Patient details are summarized in Table 1, grouped by younger (5.00-6.92 years) and older (7.0-9.25 years) ages, in anticipation of differences in hand movement control strategies, at least in the visually normal children at these matching ages^{12-14,21}. In brief, 19 of the patients had 'pure' anisometropia (>1D interocular difference in the most ametropic meridian) and 36 were strabismic (including microtropia and 4 of mixed type). The severity of amblyopia present, as quantified by the range and mean inter-ocular difference (IOD) in logMAR VA between the affected and dominant eyes, was similar in the two age-groups (t-test, $p=0.5$). Around 20% of the children in each group no longer had amblyopia, as conventionally defined, since their IODs were less than 2 lines (i.e., <0.20 logMAR). These subjects were initially labeled as 'cured', with others designated as having 'mild' or 'moderate' amblyopia, based on IOD values of 0.20-0.39 and 0.40-1.10, respectively. A similar proportion (20%) of the 7-9 year old patients (all anisometropic) had stereoacuity thresholds of 50-85 arc secs indicating that their binocular vision had recovered (2 were also no longer amblyopic) and were initially classed as having 'cured' stereovision – as was one 1 child with moderate amblyopia among the 5-6 year-olds – with the rest classified as having 'coarse' (100-600 arc

secs), 'gross' (3000 arc secs; Fly only) or 'nil' stereovision. Pilot data were obtained from 4 additional amblyopic children (2 anisometric; 1 mixed; 1 strabismic) studied longitudinally on 2-3 separate occasions before and/or during their normal treatment regime. Control children at ages 5.33-6.92 (n=13) and at 7.0-9.08 (n=15) years met inclusion criteria by having normal or corrected-to-normal VA in each eye with IODs <0.20 (respective means were 0.03 (\pm 0.06 sd) and 0.01 (\pm 0.07 sd) logMAR), stereo-thresholds of \leq 85 arc secs, and no history of ocular disorder. Informed consent/assent was obtained for participation, and conduct was in accordance with the Declaration of Helsinki and both National Research Ethics Service UK and Senate Ethics Committee of City University London approval.

[Table 1 & Figure 1, near here]

Apparatus and hand movement recordings

Participants reached for and precision grasped cylindrical household objects of 'small' (24 mm) or 'large' (48 mm) diameter, but similar (100 mm) height, placed at a 'near' midline or at two 'far' locations (10° across their midline or 10° uncrossed) with respect to the start position of their preferred hand (see Fig.1). Handedness was assessed with the abbreviated (10 question) version of the Edinburgh inventory³⁴. Children ticked the answers themselves following explanation of each question by the experimenter and, in fact, the preference expressed was always the hand in which they held the pen to complete the test. Two sets of target distances were used scaled according to the child's arm length. Lightweight (<5 g) infra-red reflective markers were placed on the wrist and tips of the thumb and index finger of this hand, and on top of the centre of each object. Instantaneous marker positions in the three-dimensions of their resultant movements were recorded (at 60 Hz) throughout each movement by 3 infra-red motion capture cameras (ProReflex, Qualisys Sweden), with spatial tracking errors of <0.4 mm. Subjects sat with eyes closed between trials and, following a verbal 'go' signal, were required to open their eye(s) and reach out "as naturally and accurately as possible" to pick up the object "at about half its height, using a precision grip", place it to one side and return to the start position. All participants performed several (typically 2-4 per view) practice movements to a neutral object placed at random table locations prior to the start of the testing, to ensure that they understood these instructions and were comfortable with the general task conditions. They then performed 12 or 18 experimental trials (i.e., 2 object sizes x 3 locations, each repeated 2 or 3 times) in separate blocks with both eyes open or with a patch occluding their dominant or non-dominant eye, these being

established for the control subjects by simple sighting *versus* non-sighting eye tests. Participants wore any habitual (i.e., most recent prescription) glasses when performing the tasks, with the patch placed under their glasses during monocular testing. Object presentations were in the same pseudo-randomized order for each of the viewing conditions, which were counterbalanced between subjects in each group.

Hand movement analyses

Analyses focused on 7 kinematic and 7 'error' measures that reflect different aspects of the efficacy of movement planning or of on-line control, several of which were seen to be defective among the amblyopic children of our earlier study²¹. Five *kinematic* measures related to the movement *dynamics*. These were: (1) the overall movement durations (from leaving the start position to picking up the object); (2) the time to peak velocity after movement onset (a measure of reach planning); the proportions (percentages) of the movement duration spent (3) in the 'low velocity' final approach (feedback) phase of the reach (between its peak deceleration and initial object contact) and (4) in the final post-contact (feedback) phase of the grasp (between initially touching the object and picking it up); and (5) in the actual time spent closing the grip (between its peak aperture at initial hand opening and the first moment of object contact). Two further *kinematic* parameters concerned *spatial* indices of grasping performance: (6) the peak grip aperture between thumb and finger (a measure of planning accuracy in preparation for grasping the target); and (7) the grip size at initial object contact (an index of end-point accuracy). Error measures related to the *reach* were; (1) late velocity corrections; (2) object collisions; and (3) spatial path (trajectory) corrections, indicative of undershooting, overshooting and misdirection of the reach, respectively. The *grasp* errors were; adjustments to the grip occurring (1) just before object contact or (2) during grip application; (3) excessively wide grips at initial contact; and (4) prolonged grip applications, indicative of inaccurate (errors 1-3) or uncertain (error 4) performance. An example of a misdirected reach is shown in Figure 4B; readers are referred to our previous, open-access publications^{10, 11, 21} for depictions of the other error-types.

Statistical analyses

Median values of the above 7 kinematic parameters along with the frequency of total reach and grasp errors and of the 7 specific error-types committed during the (12 or 18) movements

performed under each viewing condition were calculated for each subject and analyzed using IBM SPSS package version 21 (IBM Corporation, Armonk, NY, USA). Initial analyses were undertaken by repeated measures ANOVA (Huynh-Feldt corrected for lack of sphericity, when necessary) with view (binocular, dominant eye, non-dominant eye) as the within-subjects factor and with Group (controls, patients) as the between-subject factor in each age-range. *Post hoc* tests were conducted with the Bonferroni adjustment for multiple pair-wise comparisons to examine the origin of any main within-subject effects of view – with the (unadjusted) Least Significant Difference (LSD) test applied in cases where this yielded no explanation (see Key; Table 2) – followed by 1-way ANOVA to examine between-Group differences under each separate view. Subsequent comparisons by age-range were then carried out to assess possible factors (i.e., depth of amblyopia, stereovision loss, treatment history) contributing to the generally poorer performance of the patients. To provide adequate numbers in each patient sub-group for these purposes, we condensed the original classifications (Table 1) into 3 sets of just 2 ordinal categories. Specifically: for amblyopia severity, those originally labelled as ‘cured’ or as ‘mild’ were combined into a single ‘Mild’ category for comparison with the ‘Moderate’ class; for stereovision, those with ‘cured’, ‘coarse’ or ‘gross’ stereo-thresholds (Table 1) were combined into a single stereovision present (or ‘Stereo+’) category for comparison with the ‘Stereo Nil’ patients; and for treatment stage, those who had only completed refractive adaptation and/or some occlusion therapy were classed as treatment ‘Ongoing’ for comparison with those in ‘Follow-Up’ who were no longer undergoing treatment of any kind. The significance level was set at $p < 0.05$.

Two further approaches were taken to assess the impact of these factors in each patient age-group. First, preliminary stepwise (hierarchical) multiple regression analyses were undertaken to evaluate relations between the 3 sets of ordinal categories above and their potentially unique (or combined) contribution(s) to the patient deficits. We say ‘preliminary’ because the patient sample sizes were relatively low for this type of analysis. To counter this, we report adjusted R^2 values to indicate the proportion of the variance in the data attributable to the specific ordinal factor in question, their beta coefficients (indicating the unique contribution of that variable when overlapping effects of any other factors are removed statistically), and the t-statistics representing the significance of that contribution. Potential for a unique contribution was confirmed by Spearman’s rank order correlation analyses, which revealed no significant associations between any set of the variables at either age. This

included only a general tendency – as might be expected – for the patients still undergoing therapy at 5-6 ($P=0.23$, $p=0.23$) and 7-9 ($P=0.11$, $p=0.59$) years to have a greater VA loss than those who had completed it. In fact, *average* IODs were in the lower range of Moderate amblyopia in the former sub-groups of patients at the two ages (both, coincidentally, 0.50 ± 0.3 sd) and in the upper Mild category in those sampled at follow-up, this difference not quite achieving statistical significance at ages 5-6 (0.31 ± 0.2 sd, $p=0.056$) and not significant at 7-9 (0.37 ± 0.2 sd, $p=0.24$) years, and with no relationships at all between the patient's stereovision and their VA loss or treatment stage. In accordance with this, co-linearity diagnostics derived from the regression models routinely confirmed that the three ordinal variables were largely independent by consistently yielding very low variance inflation factor (VIF) scores of <1.1 . Second, Spearman's correlation analyses were conducted between each hand movement index and the stereoacuity thresholds recorded in each of the patients in which it was measurable and their IOD in VA, to determine whether the *levels* of stereovision or VA loss present in individual subjects – rather than just across broader categories – were associated with progressive reach-to-grasp effects at each age-range.

RESULTS

Overview

Tables 2 and 3 summarize the kinematic and error data obtained from the children in the two age-ranges and results of ANOVA conducted by viewing condition for each parameter within- and between-subject groups. Control children at both ages exhibited significant binocular advantages for most parameters, including key measures of their movement speed (e.g., total durations) and accuracy (e.g., grip sizes at object contact; reach and grasp error-rates). That is, *post hoc* comparisons of the main effect of view showed that these movement components were performed better when using binocular vision compared to their dominant or their non-sighting eyes alone, with the advantages being relatively small for kinematic measures (range ~5-20%; Table 2), but much more marked for error-rates (range ~33-200%; Table 3). Such binocular advantages over the dominant ('better') eye were absent among the 5-6 year-olds with amblyopia and involved only one parameter – marginally (~70 ms) shorter movement durations – in the 7-9 year-old patients, since the few other main effects of view in these

subjects were due to poorer performance *only* with their amblyopic eye (Tables 2 & 3) relative to binocular viewing.

There were numerous other differences (involving 14 of the 16 parameters examined) between the 5-6 year-old control and amblyopic subjects, with only one indicative of worse performance by the normal participants. The 7-9 year-old children with amblyopia, by contrast, showed few significant differences (on only 3 measures) compared to their age-matched normally-sighted peer-group (Tables 2 & 3). As will be seen, however, this implied improvement in eye-hand coordination abilities with age in amblyopic children was partly due to different age-related reach-to-grasp strategies adopted by the control *versus* patient groups, as well as to a developmental progression in the beneficial effects of recovered binocular stereovision in the amblyopic subjects.

[Tables 2 & 3, near here]

Age- and vision-dependent differences in overall movement times

Total movement durations in the 5-6 year-old patients were much (~200-250 ms or ~20-30%) longer than those of the age-matched controls across each of the three views, with evidence that significantly prolonged periods spent in both the early, planned (e.g., time to peak velocity) and later, guidance (e.g., grip closure times) movement phases contributed to this main effect of Group. Separate ANOVA by each ordinal patient category revealed significant relationships between total movement durations and amblyopia severity, stereovision (see Fig.2A) and treatment stage, but no interactions with viewing conditions. More specifically, *post hoc* analyses showed that patients with Moderate amblyopia ($p < 0.001$) or who were Stereo Nil ($p = 0.003$) or whose treatment was ongoing ($p = 0.02$) produced slower movements across all three views than control children, with prolonged movements also associated with Moderate compared to Mild amblyopia ($p = 0.027$). Regression analysis supported these findings, in that models examining the influence of the three ordinal variables in the patients indicated that their severity of amblyopia alone accounted for most of the variance in their movement durations under binocular (adjusted $R^2 = 0.16$, $\beta = 0.43$, $t = 2.5$, $p = 0.017$), dominant eye (adjusted $R^2 = 0.14$, $\beta = 0.38$, $t = 2.2$, $p = 0.041$) and non-dominant/affected eye (adjusted $R^2 = 0.13$, $\beta = 0.40$, $t = 2.3$, $p = 0.027$) conditions, although the models were *improved* for each view (e.g., all three now $t > 2.5$, $p < 0.015$) when further significant contributions of their stereo loss (but not treatment) were added to the stepwise analysis. Broadly similar findings applied,

as well, to the patient's prolonged grip closure times, but not to their delayed time to peak velocity which was significant only for non-dominant eye conditions in the Stereo Nil subjects.

By contrast, there was no equivalent overall Group difference in movement durations between the children aged 7-9 years nor any main effects of amblyopia, stereovision or treatment stage. But there was a stereovision x view interaction ($F_{(4,74)}=3.9$, $p=0.006$). This arose because, like the control subjects, the patients who were Stereo+ exhibited a binocular advantage over monocular viewing (of ~15%; Fig.2B) for this parameter, while the Stereo Nil participants did not. The absence of an overall Group difference was, therefore, partly driven by the similarities in binocular movement times between visually-normal and stereo-recovered subjects, along with similarities in performance by all participants when using one eye alone. Regression analysis supported these findings too, by indicating that the degree of stereovision present in the patients was uniquely sufficient to account for their binocular movement durations (adjusted $R^2=0.18$, $\beta=0.48$, $t=2.7$ $p=0.015$). Unlike in younger subjects, there were no main effects or interactions for times to peak velocity or grip closure.

[Figure 2, near here]

Age-dependent changes in reach and grasp strategies

Age-related between-group differences in approach to the tasks contributed to these effects. Most notably, there was a major change in behavior among control children who, at 5-6 years, spent only ~20% of their total movement time across all views in the low velocity/visual feedback phase of the reach, compared to ~30% at ages 7-9 (Table 2). Indeed, Spearman's correlation analysis revealed a moderate positive correlation between this reach parameter and their continuous ages (5.33-9.08) in years ($P=0.42$, $p=0.025$), such that this aspect of on-line reach control in the older children, including their small binocular advantage – at least over the non-dominant eye (of ~13%) – began to resemble that of normal adults¹⁰.

The 5-6 year-old children with amblyopia, however, appeared to place as much reliance on visual feedback as the normal 7-9 year-olds, since they too spent a similarly greater proportion (~32%) of their movements in the low velocity reach phase across all views compared to their age-matched controls. Indeed, it was the much longer period of *actual* time (some 150-175 ms) spent by the younger patients finally approaching the targets that accounted for most (70-75%) of the between-Group difference in movement durations at this age (Fig.2A). It was also mainly the normal change in reach strategy that eliminated any

between-Group difference at ages 7-9 years, although the patients appeared to contribute to this via a small *reduction* in relative approach times (of 3.3%) after ages 5-6.

There was also an important age-dependent change in grasping strategy related to the percent time spent in contact with the object before it was lifted but, in this case, mainly involving the older children with amblyopia (Table 2). Specifically, whereas all control subjects and the younger patients spent equivalent relative periods of time (~15%) in this movement phase across all views, the 7-9 year-old children with amblyopia increased their post-contact times to a mean of 17.4%, this increase being significant relative both to the younger patient counterparts ($F_{(1,53)}=5.0$, $p=0.03$) – although not quite correlating with age (5.0-9.25) in years (Spearman's $P=0.21$, $p=0.10$) – and to their age-matched controls. Indeed, it was the relative increase in *actual* post-contact time (some 30-50 ms) by the older patients that accounted for most (~80%) of the between-Group difference in movement durations at ages 7-9 (Fig.2B).

[Figures 3 & 4, near here]

Stereovision-dependent benefits for reaching performance

The 5-6 year-old children with amblyopia made significantly more total reaching errors than their age-matched controls (Table 3) particularly when using both eyes, but also under dominant and non-dominant eye conditions. These differences were due to increased rates of late corrections to the reach velocity (i.e., 'undershoots') and, most markedly, to its spatial path by the patients, whereas the 5-6 year-old control children – uniquely among all subjects groups – produced more high-velocity collisions with the objects (i.e., over-shoots) when viewing monocularly, consistent with their distinctively ballistic reaching behavior. ANOVA showed main effects of stereo loss on total reach errors (Fig.3A), late velocity and spatial path corrections (all $F_{(2,40)}>3.0$, $p<0.05$), due to their increased occurrence in the Stereo Nil compared to control subjects and compared to the Stereo+ participants in the cases of total reach and spatial path errors. There were no equivalent effects of amblyopia or treatment. Regression analysis suggested that stereovision loss was the sole factor responsible for the increased total reach errors in these patients under binocular (adjusted $R^2=0.16$, $\beta=0.50$, $t=3.0$, $p=0.007$), dominant eye (adjusted $R^2=0.14$, $\beta=0.43$, $t=2.5$, $p=0.020$) and non-dominant/affected eye (adjusted $R^2=0.13$, $\beta=0.48$, $t=2.9$, $p=0.007$) conditions and for their misdirected reaches across all views (adjusted $R^2\geq 0.25$, $\beta\geq 0.53$, $t\geq 3.30$, $p\leq 0.003$), but provided no model explaining their increased late velocity corrections.

There was no overall between-Group difference in total reach errors in the older children (Table 3). But there were main effects of stereovision ($F_{(2,37)}=4.8$, $p=0.014$) and a stereo x view interaction ($F_{(4,74)}=3.3$, $p=0.015$). These were due to consistently more error-prone performance, particularly in misdirected reaching (see Fig.4B), by the Stereo Nil compared to control and Stereo+ subjects, combined with an obvious binocular advantage (of ~33-50%), similar to the controls (~45-60%), among those who were Stereo+ (Fig.3B). Stepwise regression models indicated that stereovision loss was the only significant contributor to the increased total reach errors in these patients with binocular (adjusted $R^2=0.15$, $\beta=0.43$, $t=2.5$, $p=0.019$), dominant eye (adjusted $R^2=0.14$, $\beta=0.41$, $t=2.2$, $p=0.048$) and non-dominant/affected eye (adjusted $R^2=0.25$, $\beta=0.58$, $t=3.2$, $p=0.004$) viewing, and to the increased spatial path errors in the binocular condition (adjusted $R^2=0.17$, $\beta=0.50$, $t=2.6$, $p=0.016$). Thus improved reaching accuracy, indicative of better target localization, were consistent benefits of stereovision across both subject ages and groups.

[Figures 5 & 6, near here]

Stereovision-dependent benefits for grasping performance

Normal binocularity provided additional benefits for grip planning. Control children of both ages formed significantly wider initial peak grip apertures with monocular viewing (Table 2), an effect typically associated with an increase to its 'safety margin' produced by normal adults under similar conditions of increased visual 'uncertainty'⁷⁻¹¹. But this cautious approach was absent in the patients who produced virtually identical peak grips at both ages across all views. The aperture of the peak grip usually increases quite linearly with increasing target size and, in fact, all participants did this, by a factor of x0.84-0.89 when preparing to grasp the 'large' compared to 'small' object. This relative scaling behavior was, however, closer to the normal adult mean (of x0.82³⁵) in the control children who, as exemplified in Figure 5, also showed significant view x object size interactions, in which they produced wider monocular peak grips *only* for the smaller object, as normal adults do on our task¹⁰. But the patients did not, suggesting that they were equally 'uncertain' when planning to grasp the smaller object when using two eyes as with one eye alone.

Despite these effects, there were no between-Group differences at either age in the grip size achieved on initial contact with the objects (Table 2). Moreover, all subjects made contact with the smallest grip sizes closer to the average width of the two targets (=36 mm)

when viewing binocularly, an improvement in accuracy that was independent of the object's size, although only significant in relation to poorer amblyopic eye performance by the patients.

For the control children, the suggested binocular advantage for grip precision was supported by their reduced total grasp error-rates when using both eyes and, particularly, in their need to make fewer subsequent adjustments to their grip after object contact (Table 3). The amblyopic children, however, generally committed more grasping errors than the controls and showed no evidence of a binocular advantage for reducing post-contact grip adjustments. Indeed, total grasp error-rates in the patients aged 5-6 were roughly doubled across all views compared to the matched control Group and involved increases in every sub-type of 'inaccurate' and 'uncertain' grasping measure (see Methods). There was also a main effect of view for cumulative grasping errors in this patient cohort, mainly due to the increased occurrence of abnormally wide (i.e., inaccurate) grips at initial object contact under amblyopic eye compared to binocular viewing, consistent with the above findings related to their 'grip size at contact' (Table 2), for which this is a related 'error' parameter. There were no other significant effects, including of stereovision loss (Fig.6A), or interactions with view.

In contrast, total grasping error-rates were similar in the 7-9 year old patients *versus* controls, although abnormally prolonged contacts with the objects were more common in the amblyopic children across all views, this partly reflecting their increased 'post-contact times' (Table 2). The patients also more frequently adjusted their grip just before object contact and made contact with abnormally wide grips under amblyopic eye compared to binocular viewing. Additional ANOVA, however, revealed a main effect of stereovision ($F_{(2,37)}=5.3$, $p=0.010$) and a stereo x view interaction ($F_{(4,74)}=2.8$, $p=0.034$) for cumulative grasp error-rates. These were, again, due to consistently worse performance – particularly in producing abnormally wide grips at contact – by the Stereo Nil compared to control and Stereo+ subjects, combined with a small binocular advantage (of ~22%) relative to control subjects (~70-90%), among those who were Stereo+ (Fig.6B). Stepwise regression models indicated that stereovision loss was the only significant contributor to the increased total grasp errors in these patients when using binocular vision (adjusted $R^2=0.18$, $\beta=0.43$, $t=2.3$, $p=0.032$) – but not either eye alone – and abnormally wide binocular grips at contact (adjusted $R^2=0.21$, $\beta=0.47$, $t=2.5$, $p=0.021$). Thus improved grasping accuracy, indicative of better end-point control, were consistent benefits provided by stereovision across subject ages and groups.

Correlation analyses

Among the 12 younger Stereo+ patients (Table 1) there were small-to-moderate positive Spearman's correlations ($P=0.32-0.60$) between progressive increases in their IODs in VA and movement durations, total reach error-rates and grip sizes at contact across all views, but only the correlation between grip size and amblyopic eye viewing achieved significance ($p=0.039$). Increases in total reach error-rates across all views ($P=0.57-0.69$, $p<0.05$) and in grip size at contact with binocular viewing ($P=0.73$, $p=0.007$), however, were moderately-to-strongly associated with increasing stereo-thresholds in this patient sub-group, in line with some of the foregoing analyses. However, there were no significant correlations between either IODs or stereo-thresholds for any movement parameter across the 14 Stereo+ subjects at 7-9 years of age.

[Table 4, near here]

The 'cured' stereovision and longitudinal cases

'Treatment stage' was never found to be a significant factor in our regression analyses, implying that the patients' therapeutic history *per se* had little or no impact on their reach-to-grasp abilities. However, average data obtained from the 5 older patients (all anisometropes) with 'cured' stereoacuties (3 of whom had residual mild or moderate amblyopia) were all within the upper bound 95% confidence limits of (i.e., indistinguishable from) age-matched controls. As indicated in Table 4, key movement time and total error measures in the 4 patients studied longitudinally at different stages of their treatment also suggested that this can benefit eye-hand coordination, *provided* it results in binocular recovery. Specifically, the initial performance of the two anisometropic cases (A1, A2) whose stereovision was essentially normal at treatment cessation improved markedly, culminating in binocular advantages for both movement speed and accuracy within the normal range. But this did not occur in either the mixed (M1) or strabismic (S1) cases whose amblyopia severities were, respectively, mild and 'cured' at the end of their therapy, but who remained 'stereoblind' throughout. The following two cases highlight these differences.

[Figures 7 & 8, near here]

Case A1: binocular recovery, but persistent moderate amblyopia. This patient initially presented at age 7.8 years with marked anisometropia (R eye +8.25/-1.50x180; L eye +2.00/-0.25x180) and severe amblyopia (R eye VA 2.00 logMAR, IOD 1.88). Cover test revealed an exophoria, and there was complete R eye Bagolini lens suppression with Nil stereovision. He

was first tested (uncorrected) on the day before he received his spectacles (Untreated), when his reaching and grasping movements were notably slow and inaccurate, especially when using the amblyopic eye (Fig.7). Repeat testing occurred immediately after 3.5 months of refractive adaptation and, finally, 8 months later (aged 8.75 years) following part-time (4 hrs/day) occlusion therapy with which he was reported to have been compliant, but had just been withdrawn due to signs of decompensation (i.e., cover test showed a flick R exotropia). Following spectacle correction his amblyopia was moderate (VA 0.78, IOD 0.78) and was associated with a dramatic improvement in both his stereovision (to 100 arc secs) and reach-to-grasp performance across all three views, although the data obtained in the binocular condition were all beyond the upper 95% confidence limits of those in matched control subjects. However, after further gains in VA (to 0.54, IOD 0.52) and in stereoacuity (to 60 arc secs) following occlusion therapy, there was evidence of binocular advantage, such that his eye-hand coordination abilities were indistinguishable from those of the control subjects (and from his normally-sighted older brother, who we tested at age 9.3 years).

Case M1: absent binocularity, with mild amblyopia. This patient initially presented at age 5.8 years with marked anisometropia (R eye +1.00/-0.25x180; L eye -8.00/-0.50x30) and strabismus. She had moderate-to-severe amblyopia (L eye VA 1.00 logMAR, IOD 0.85) and absent stereovision with complete L eye suppression. She was first tested at age 6.2 years after 4 months of spectacle correction and, again, at follow-up aged 7.5 years, 3 months after completing a year of prescribed occlusion (5 hrs/day) with which she was reported to have been reasonably compliant, but was no longer showing improvement. Her L eye VA had improved after refractive adaptation (0.62 logMAR, IOD 0.62) and after occlusion (0.36; IOD 0.34), so that she still had mild amblyopia at the end of her treatment. But her lack of stereovision remained unchanged, as did her eye-hand coordination abilities (Fig.8), which were persistently poorer than that of matched controls and showed little evidence of binocular advantage, except compared to her amblyopic eye performance. Note that, as with case S1, there was also little evidence of a learning effect on our tests between her visits (Table 4), supporting the view that the improved performance of patients A1 and A2 were associated with their stereo-recovery rather than due to simple task-specific practice.

DISCUSSION

Binocular vision normally provides essential 3D spatial information for improving the initial planning and subsequent guidance of reach-to-precision grasp movements. Commensurate with this, removing binocular information (e.g., from vergence and disparity⁷⁻¹¹) by covering one eye in our normally-sighted children resulted in slower, yet less accurate, movements. We interpret this as due to ‘uncertainties’ under these reduced-cue conditions about the precise location and intrinsic 3D properties (size, shape, curvature) of the cylindrical goal objects during encoding of these features for respective planning of the reach and the grasp, and when attempting to monitor relative depth changes between the moving hand/digits and intended end-point grip positions on the objects in the guidance phase. Restricting vision to one eye also resulted in generally greater performance deficits relative to habitual binocular viewing in the older compared to younger control children, consistent with previous findings of increasing binocular advantage, especially in on-line control, for improving eye-hand coordination with age^{4-14,21}. In anticipation of this and of impaired reach-to-grasp abilities in amblyopic children with naturally degraded binocular 3D vision²¹, the present study addressed two main questions. Do the impaired abilities in amblyopic children relative to matched controls also change with age between 5-6 and 7-9 years; and are they mainly related to their reduced visual (spatial) acuity in the affected eye or defective stereovision?

Age-related differences

The answer to the first question is clearly ‘yes’. Although not necessarily in the expected direction, because differences in reach-to-grasp performance were much more marked, regardless of viewing condition, in the 5-6 year-old children with amblyopia compared to control subjects than between the older patient and control groups. A key reason for the marked differences at ages 5-6 was that, in agreement with previous findings, the normal children appeared to use vision mainly for feedforward (planning) of their hand movements^{12-14,21}, whereas the patients adopted a more balanced dual-strategic approach, spending longer than the controls in the early planned (e.g., time to peak velocity) phase of their reach, but much longer in its later ‘in-flight’ visual feedback (guidance) period. This suggests that 5-6 year-olds with normal 3D spatial vision are sufficiently confident that the information it provides for target localization during reach preparation will be adequate to achieve the desired outcome and/or satisfied to accept the ‘cost’ of occasional errors (e.g., collisions with

the object; Table 2) that might have been rectified by more use of feedback, whereas amblyopic children of the same age are not. We conclude from this that their degraded 3D vision generates uncertainty about object location and size/shape at the planning stage, of which they may well be consciously aware. This, in turn, causes them to slow down during movement execution and to engage in frequent on-line corrections of their initial misreaching (e.g., in required distance or direction; Fig.4B) and subsequent grasping errors, while attempting to do this using degraded visual feedback information as well.

Our results further suggest that problems associated with visually encoding these spatial target properties during movement preparation were not completely resolved in the 7-9 year-old patient cohort. This was because they, too, made numerous corrections to their reach path and also appeared to adopt (consciously or otherwise) a compensatory grasping strategy across all views of prolonging their grip contact with the objects prior to lifting them (Tables 2 & 3). We have previously²³ observed similar selective increases in post-contact times among stereo-reduced adults and found that they were related to significant increases, compared to controls, in trial-by-trial variability of their initial digit placements when repeatedly grasping the same objects, this imprecision being especially marked along the *depth* axis of the targets. We argued that the prolonged contacts were likely designed to acquire extra tactile and kinesthetic feedback from the digits, so ensuring that they were appropriately positioned to apply the grip forces necessary to lift the objects and that such a cross-modal sensory adaptation represented a sensible mechanism to compensate for variable errors in visually guiding the thumb (especially^{23,36}) and finger to the optimal object contact points for this subsequent purpose.

The current data would, therefore, suggest that this strategy is also implemented by amblyopic children as young as 7-9 years, presumably to counter problems of end-point uncertainty they had already experienced in trying to use vision to plan and guide their grasps earlier in life. Indeed, increased reliance on non-visual information for motor control may be a general response to amblyopia, because – anecdotally – we had to persuade several of our current patients not to employ another tactile/kinesthetic compensation for their reaching difficulties during the initial practice trials prior to the main testing, which involved sliding their hand along the table surface to acquire the objects. We did not analyze digit contact variability in the present work. However, the peak grip apertures formed by the amblyopic children of both ages showed evidence of ‘uncertainty’ about the spatial dimensions of the goal objects,

in that they adopted a similarly wide safety margin when preparing to grasp the smaller target under all viewing conditions and less appropriate aperture scaling for the larger object (Fig.5).

[Table 5, near here]

Advantages of recovered stereovision

The answer to the second question was slightly more mixed. Repeat measures ANOVA and regression analyses indicated that amblyopia was the main contributor to the prolonged movement durations and grip closure times of the 5-6 year-old patients across all views. But these were the only performance deficits for which the degree of VA loss was the most important factor at either age, and also showed secondary influences of their abnormal binocularity. Absence of stereovision, by contrast, was revealed as the *exclusive* factor in a wider range of the patient's deficits, including their increased reaching errors across all views at both ages, along with aspects of slower (prolonged movement durations) and inaccurate (e.g., spatial reach errors, imprecise end-point grips) binocular performance in the older children. Indeed, the effects of recovered binocularity in the 7-9 year-old Stereo+ patients appeared to provide such notable benefits for movement speed (Fig.2B) and for reach and grasp accuracy (Figs.3B, 6B) – despite their similar VA losses to those of the Stereo Nil subgroup (respective mean IODs, 0.45 ± 0.30 sd *versus* 0.40 ± 0.27 sd, $p=0.62$) – that those with stereoacuities in the normal range could not be distinguished from control subjects.

A different approach to the data, summarized in Table 5, supports these conclusions by showing each of the specific kinematic and error-type measures that were defective, according to 1-way ANOVA, under each of the three viewing conditions in the patients with different VA *versus* stereovision losses compared to the matched controls. At both ages, deficits in performance occurred with almost equal likelihood in those with Mild compared to Moderate amblyopia, whereas they were much more common in the Stereo Nil than Stereo+ patients aged 5-6, with the Stereo Nil 7-9 year-olds also having the worst binocular performance. That is, this alternative approach indicated that the severity of stereovision loss was a better predictor of the patient's eye-hand coordination skills at both ages than their degree of amblyopia. Evidence from the prospectively studied cases (Table 4) points to this same conclusion, since it was the 2 patients (M1, S1) with unmeasurable stereovision at the end of their therapeutic regime whose reach-to-grasp abilities did not appear to benefit much from treatment, despite normalization of their initial visual acuity deficits.

Profile of fine visuomotor skill development?

A surprising and important finding in our earlier study²¹ was that children with amblyopia performed worse than controls on a variety of measures when using their better (dominant /sighting) eye alone. Our current data (e.g., Table 5) confirms this finding, but only for the 5-6 year old children, which was the age-range of the majority of patients tested previously. This clarification may be clinically relevant, because it implies that difficulties initially associated with use of the dominant eye (slower movements, yet more errors) in younger amblyopic children become largely resolved by age 7-9, not in teenage years as we originally speculated. Moreover, these data further suggest that most of the initial reach-to-grasp impairments at ages 5-6 when using two eyes and even just the amblyopic eye alone also quite rapidly resolve, since there were few significant differences evident between the 7-9 year old patients and control children under these other viewing conditions as well.

This raises a further important question: given this new evidence, what accounts for that fact that we^{22,23} and others^{33,37-39} have observed eye-hand coordination deficits on a variety of 3D tasks with binocular and/or affected eye viewing in adults with persistent amblyopia or stereo-deficiency? We believe that two main factors are involved. One is the inherent within- and between-subject variability in the performance of both amblyopic and visually normal children at the ages tested here so that between-group differences of as much as 25-33% that might appear to be biologically important (e.g., binocular movement durations in Stereo+ *versus* control subjects at age 5-6, Fig.2A; object collisions at ages 7-9, Table 3) do not always achieve statistical significance due to overlapping confidence limits, whereas the more consistent behavior of both types of adult participant reduces this problem. The other is that eye-hand coordination skills continue to improve quite markedly beyond 9 years of age in the normally-sighted, but less so in amblyopic individuals. For example, comparisons of performance on equivalent reach-to-precision grasp tasks that we have conducted during the past few years imply that reach error-rates decline by factors of ~6-8x between age 7-9 years and adulthood in control subjects, but by only around 4-5x over the same developmental period in mild-to-moderately amblyopic or 'stereo-blind' patients²¹⁻²³.

The above and other existing evidence suggests that abnormal binocularity is, again, the key factor resulting in this relatively 'arrested' visuomotor development. For example, Wilson and Welch⁴⁰ examined longitudinal motor skill development, using a battery of eye-hand coordination and other tasks, in a birth cohort of ~1000 children at ages 7, 9 and 11

years, and found no differences at any age between children with amblyopia or with good post-treatment recovery of VA compared to control subjects. However, sub-dividing the same study members by their stereoacuity levels, while controlling for the presence of amblyopia, revealed direct positive correlations between their degree of reduced binocularity and delayed visuomotor skill acquisition. Correlation analyses in some other large-scale, cross-sectional studies³¹⁻³³ have revealed similar relationships between stereo-thresholds and fine motor skill development, as we did here for a few parameters in our younger, but not older, Stereo+ children. This latter failure may have been due to the stereo-thresholds of most (11/14) of these older patients being clustered over a narrow (50-200 arc secs) range and/or to variability in the data obtained from this small patient sample. Good stereovision also appears necessary to for normal visuomotor learning in adulthood. Mazyn et al⁴¹ trained control and stereo-deficient (400 arc secs or worse) adults with similarly poor baseline catching skills on a task in which they attempted to catch one-handed ~1500 tennis balls in 8 sessions over a period of 2 weeks. Control subjects increased their average catching success on the trained task by a factor of x5.4, whereas performance gains after this intensive training were only around half that among those who were stereo-reduced. This would imply that people with poor stereovision may require twice as much practice to achieve – if at all – the same motor skill levels as subjects with normal binocularity.

Mechanisms underlying normal procedural motor learning, in which continual movement rehearsal and practice – often involving cognitive effort and feedback evaluation – eventually becomes ingrained as a more automatic skill are known to involve extensive parieto-frontal cortical, basal ganglia and cerebellar networks. The visual input to this network underlying important neural transformations (e.g., internal representations) for action control mainly involves the ‘dorsal stream’ cortical system emanating from occipital visual areas and terminating in posterior parietal regions¹, many of which are specifically recruited during the stereoscopic extraction of object location and 3D properties⁴²⁻⁴⁵. These considerations may offer a general explanation for the arrested visuomotor development and performance deficits in individuals lacking the neural machinery needed to process this information and, more specifically, why our children aged 5-6 with measurable, but reduced, stereovision, including patient A1 after optical correction and patient A2 when she was first tested (Table 4), had still yet to acquire skilled control of their hand movements.

Task difficulty

Our eye-hand testing procedure involved presenting objects of two sizes at different locations in order to reduce the occurrence of over-repetitive, stereotypical, movements. But, in general accordance with Fitts Law^{46,47}, they should also vary task difficulty, whereby the larger amplitude reaches to the far locations for the smaller (less stable) object would be expected to generate more noise in the motor system and greater accuracy demands than to the near midline position for the larger target. Since it is often reported that impaired binocular performance under conditions of reduced stereopsis may be exacerbated by increased difficulty on some 3D visuomotor tasks^{11,31-33,48}, we compared the movement durations (timing) and total reach and grasp error-rates (accuracy) of the patients when they executed binocular movements under 'harder' (far-uncrossed, small object) *versus* 'easier' (near, large object) trial combinations. ANOVA revealed expected significant effects of task difficulty and of stereovision – but not of amblyopia severity – with all three parameters increasing by factors of ~x1.2-1.5 between harder and easier tasks and between Stereo Nil and Stereo+ patients. But there were no task x stereo interactions, suggesting that the Stereo Nil subjects were no more *relatively* impaired on the more difficult task than those with better binocularity.

Cause: strabismus versus anisometropia

Amblyopia due to these different underlying causes is known to result in different patterns of visual anomaly, so an obvious question is whether the two sub-types also exhibit different reach-to-grasp impairments. For example, strabismic subjects typically show greater deficits in positional acuity and spatial localization in their affected eye than anisometropic individuals with similar VA losses¹⁵⁻¹⁷. Some strabismic adults also exhibit systematic directional errors in 2D manual pointing that have been directly linked to their mislocalization problems⁴⁹. We were able to age-match only small subsets (n=7-8 each) of our strabismic and anisometropic patients by Mild amblyopia and Stereo+ binocularity or by Moderate amblyopia with similar mixtures of SA losses. Although contrary to evidence of similarly altered reach planning in adults with amblyopia independent of cause^{50,51}, ANOVA suggested that the subset of mildly amblyopic and Stereo+ anisometropic children produced significantly longer times to peak reach velocity and to complete their movements under all views than the strabismics (by ~17.5-30%) with the same (largely recovered) visual characteristics. And there were no other

cause-related differences, including in misdirected reaches (i.e., spatial path errors) that might be expected to be specifically increased among those with strabismus.

Conclusions and implications for amblyopia therapies

Our findings add to a growing consensus that the impaired performance of children and adults with a history of amblyopia on a variety of real-world visuomotor tasks, especially – but not limited to²⁰ – those with obvious 3D components is primarily related to their degree of abnormal binocularity, the reason being that use of alternative monocular visual or of non-visual information, even with practice or familiarity^{41,52,53}, cannot completely compensate for their particular difficulties in planning and/or guiding movements in the depth plane^{23,39}. This even includes apparent failure to exploit motion parallax as a potentially highly reliable alternative depth cue, since our current children, as with subjects in our previous studies²¹⁻²³, had freedom of head motion before and during their movements, a likely reason being that the neural processing times required to extract such information, as with other monocular 3D cues (e.g., texture), are too long^{9,33} to be of generalized use for the immediate demands of action control.

These considerations emphasize the benefits of recovering or improving binocular function, rather than just vision in the affected eye, in children with amblyopia. While such enhancements in stereovision occur in many individual cases via conventional treatments with glasses, occlusion and/or squint surgery, several novel approaches, involving anti-suppression^{16,54} and active perceptual learning or video game-playing⁵⁵⁻⁵⁸, have shown additional promise in this regard. However, amblyopia management needs to be carefully calibrated, and it could be that greater targeting of binocular recovery is at the detriment of restoring higher-level functions (e.g., in spatial or object vision) to the affected eye. Another caveat is that while Stereo Nil subjects are consistently revealed to have significant visuomotor deficits compared to controls, this is not so generally true of individuals with reduced (e.g., coarse) stereopsis, who may be impaired only on specific tasks, the identity of which have yet to be fully determined. It is also notable that the patients for whom recovering stereoacuity poses both the greatest challenge and risk of inducing intractable diplopia tend to be those with large-angle squint who may have been Stereo Nil for a considerable time at presentation^{28,29}. Further studies are required to better evaluate these issues and to weigh the relative benefits of targeting binocular visual recovery against the possible risks.

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Figure Legends

Figure 1: The experimental set-up showing (top) the 3 wall-mounted ProReflex infra-red motion capture cameras triangulating the (bottom) black workspace table from above. On this, the start button is in the foreground, with the 'large' object shown at a 'near, midline' location; the 'small' object at an 'ipsi, far' location (for a right-handed subject); and the neutral object used only for practice at a 'contra, far' location. The locations shown were used for children with arm lengths ≥ 35 cm; blue stickers indicate those used for subjects with shorter arms.

Figure 2: Average movement durations by age (A) 5-6 years, (B) 7-9 years, viewing condition and stereovision. Movement times increased successively between control, Stereo+ and Stereo Nil subjects at ages 5-6, but were similar in the control and Stereo+ participants at ages 7-9, including faster performance with binocular compared to monocular vision, whereas there were no differences across views in the older Stereo Nil subjects. Errors bars, SEMs.

Figure 3: Average total reach error-rates per trial by age (A) 5-6 years, (B) 7-9 years, viewing condition and stereovision. Stereo Nil subjects made the most reaching errors at both ages with no differences across the three views, whereas performance was similar in the control and Stereo+ participants, particularly at ages 7-9 with fewest errors occurring in the binocular condition. Errors bars, SEMs.

Figure 4: Profiles of (A) a normal and (B) a corrected spatial reach path during binocular movements towards the same 'near, midline' target (filled circle) in (A) a left-handed control subject aged 7.25 years and (B) a right-handed Stereo Nil patient aged 7.33 years. The origin (0) of both movements on the x-axis corresponds to the starting hand positions; solid traces show the reach paths collapsed into lateral and forward directions and terminating just short of the target (as they were recorded from the marker on the wrist). In (A) the movement of the left hand follows a typical, slightly curved trajectory in a leftward (-ve) lateral direction, but in (B) the trajectory is not a rightward mirror-image. Instead, the patient initially moved slightly rightward (open arrow), but misdirected his reach towards the midline well short of the target's location, necessitating a subsequent trajectory correction (filled arrow) – defined as a spatial path error – in order to acquire it.

Figure 5: Average peak grip apertures produced by 5-6 year old participants prior to grasping the (A) 'small' and (B) 'large' objects, by viewing condition and stereovision. Only the control subjects *selectively* opened their grip much wider when preparing to grasp the smaller object when using monocular vision, this being classically designed to increase the 'safety margin' for error under conditions of perceptual uncertainty. Error bars, SEM.

Figure 6: Average total grasp error-rates per trial by age (A) 5-6 years, (B) 7-9 years, viewing condition and stereovision. Grasp error-rates increased successively between control, Stereo+ and Stereo Nil subjects at ages 5-6, but were similar in the control and Stereo+ participants at ages 7-9, including generally better performance with binocular compared to monocular vision, whereas there were no differences across views in the older Stereo Nil subjects. Errors bars, SEMs.

Figure 7: Recovery of stereovision and eye-hand coordination deficits in a child with anisometric amblyopia (case A1). Patient data are median movement durations (12 trials per view) compared to 12 Control subjects of equivalent ages (range 7.0-8.75 years) over which the patient was tested between at initial presentation (Untreated) and the end of his spectacle adaptation (Refracted) and occlusion therapy (Occluded). For further patient details, see text. NonDom: the amblyopic eye in the patient; the non-sighting eye in the Controls. Error bars are upper bound 95% confidence limits.

Figure 8: Persistent eye-hand coordination deficits with absent stereovision in a child with mixed (anisometric and strabismic) amblyopia (case M1) at the end of her spectacle adaptation (Refracted) and at follow-up, after occlusion therapy (Occluded) compared to Control subjects. Other conventions are as in Figure 7.



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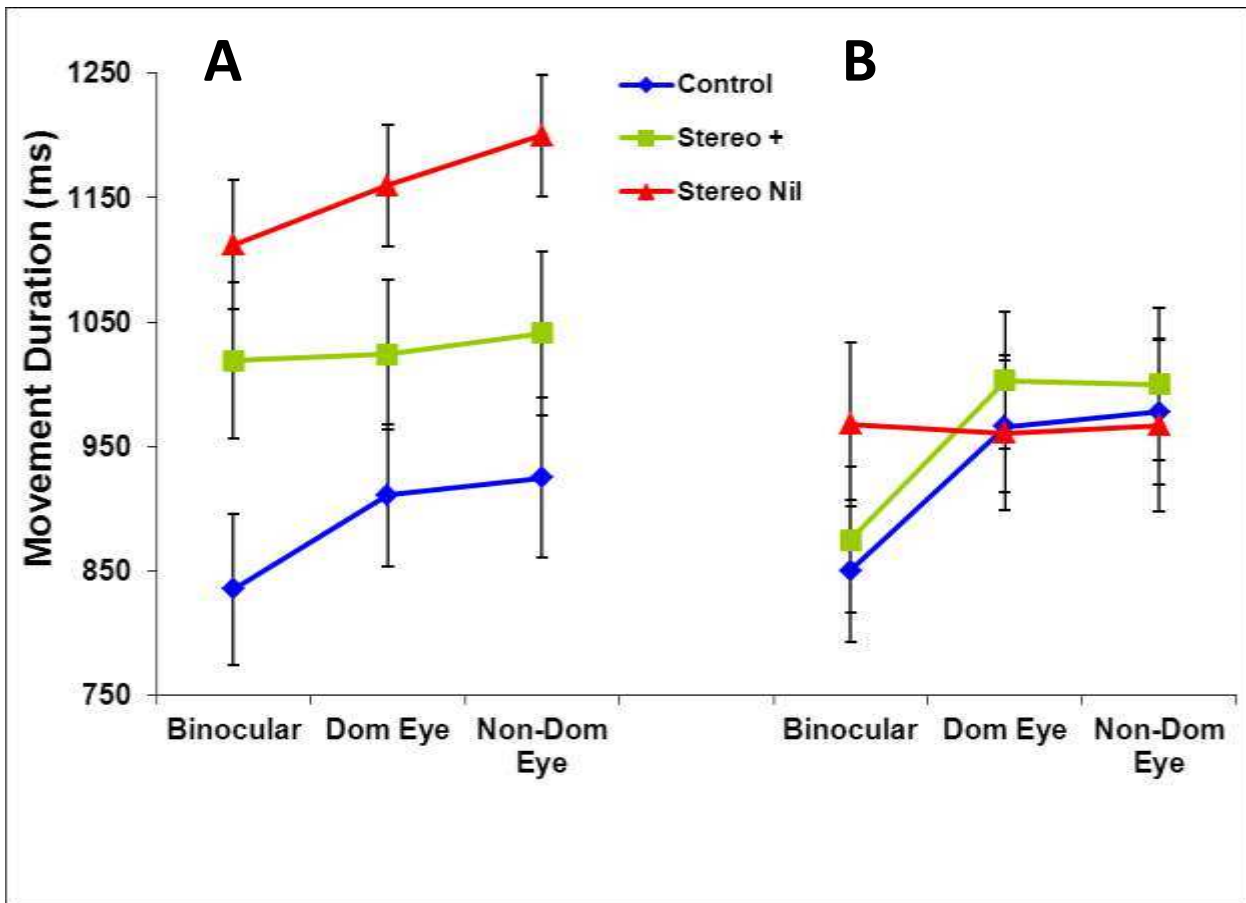


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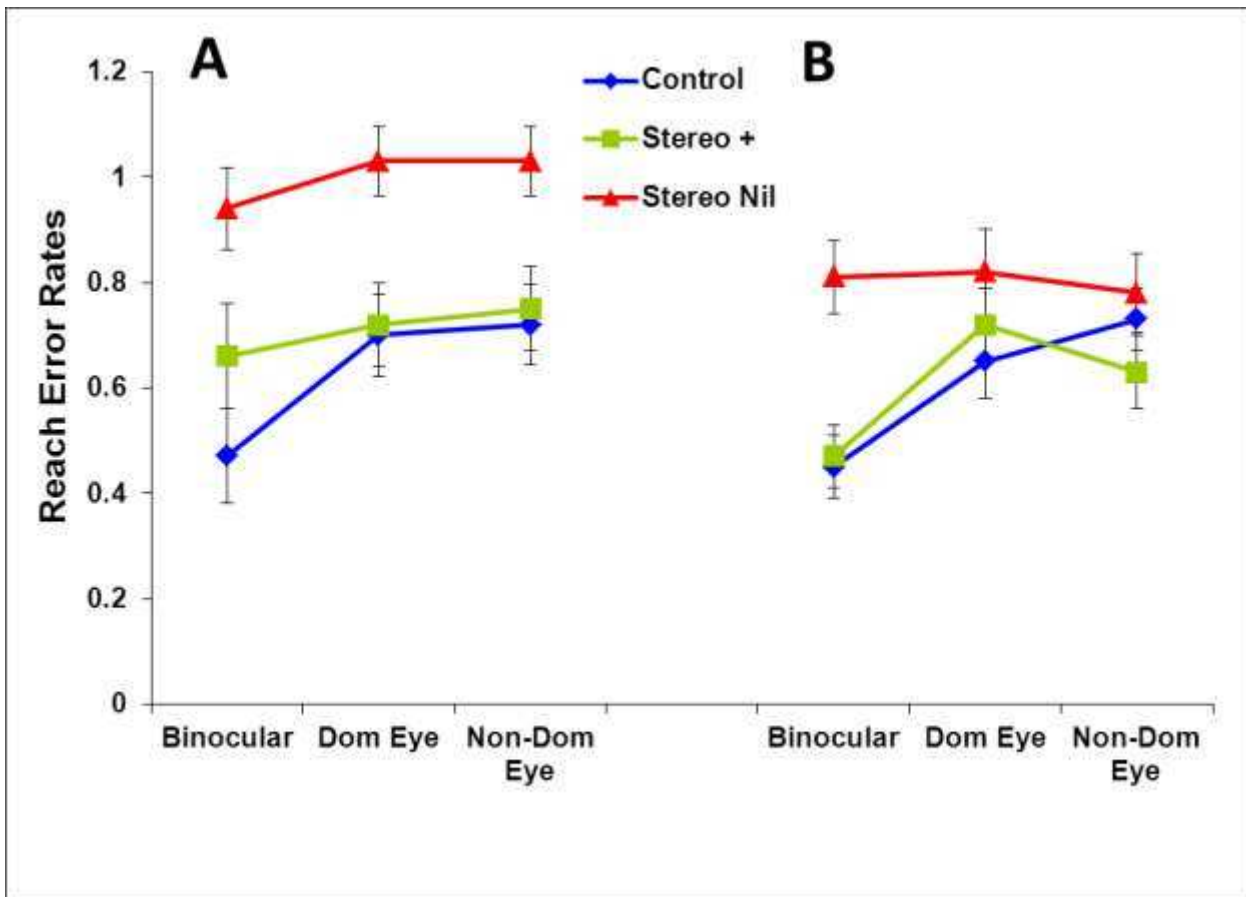


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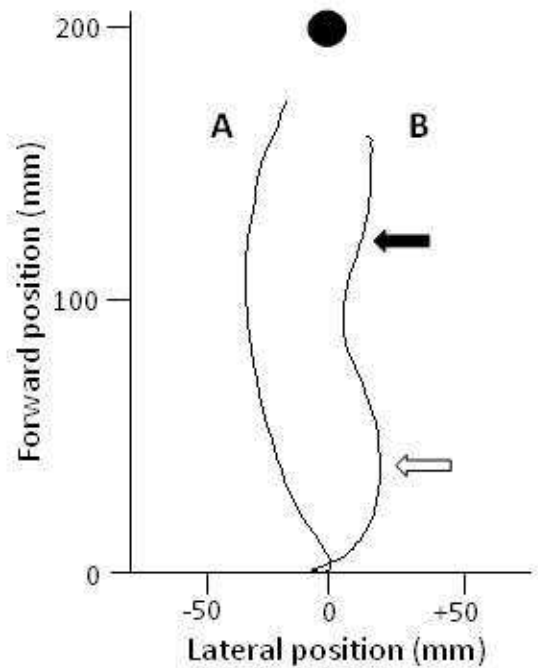


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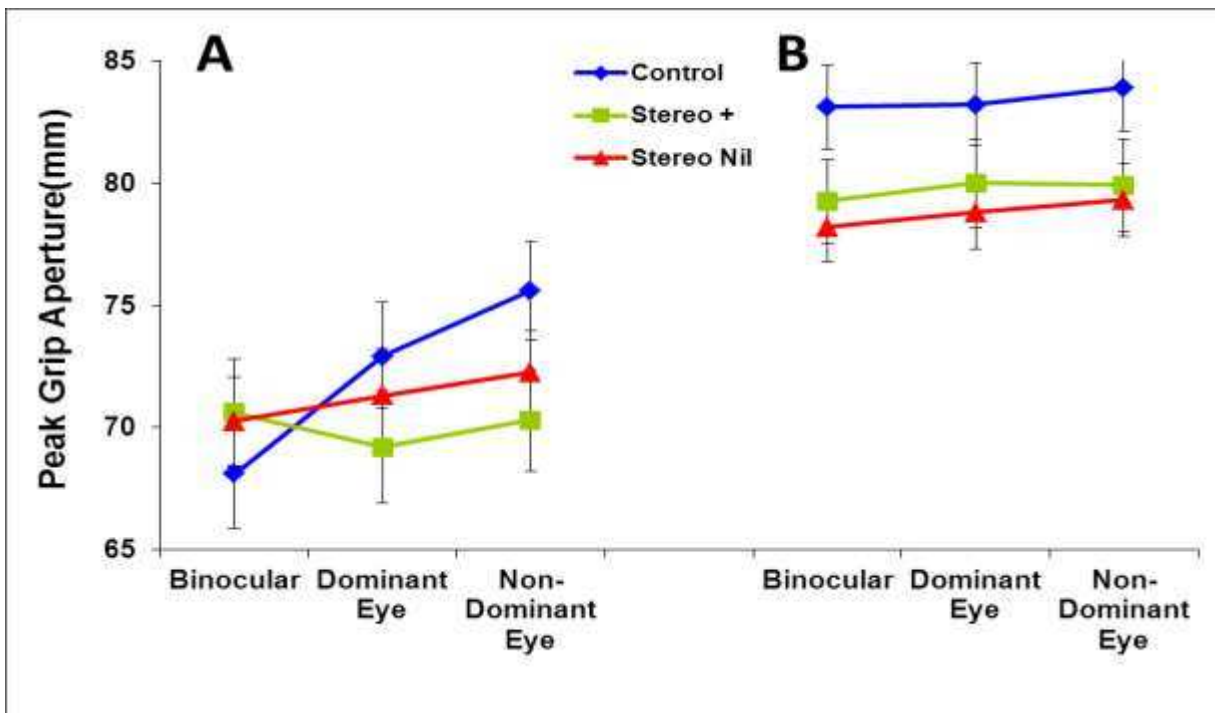


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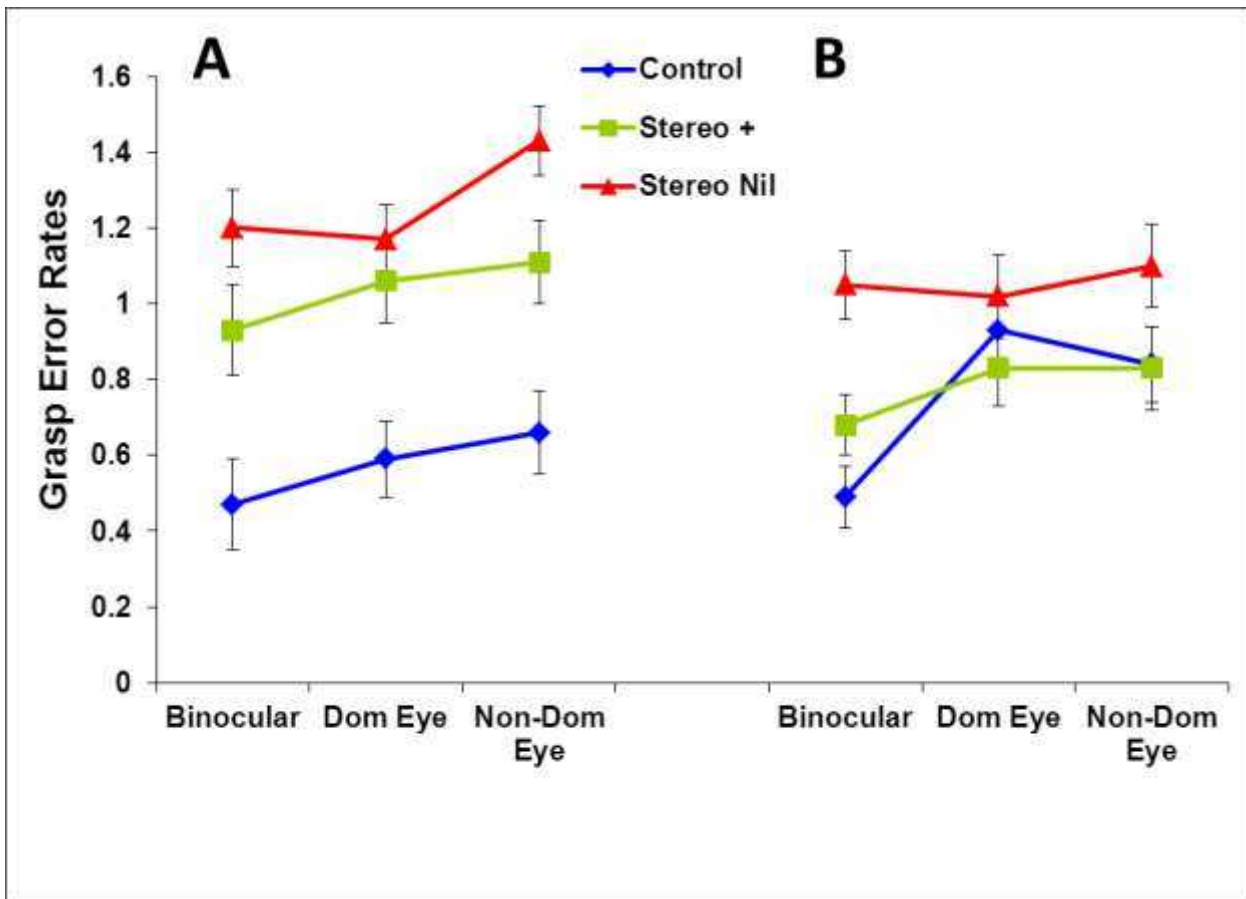


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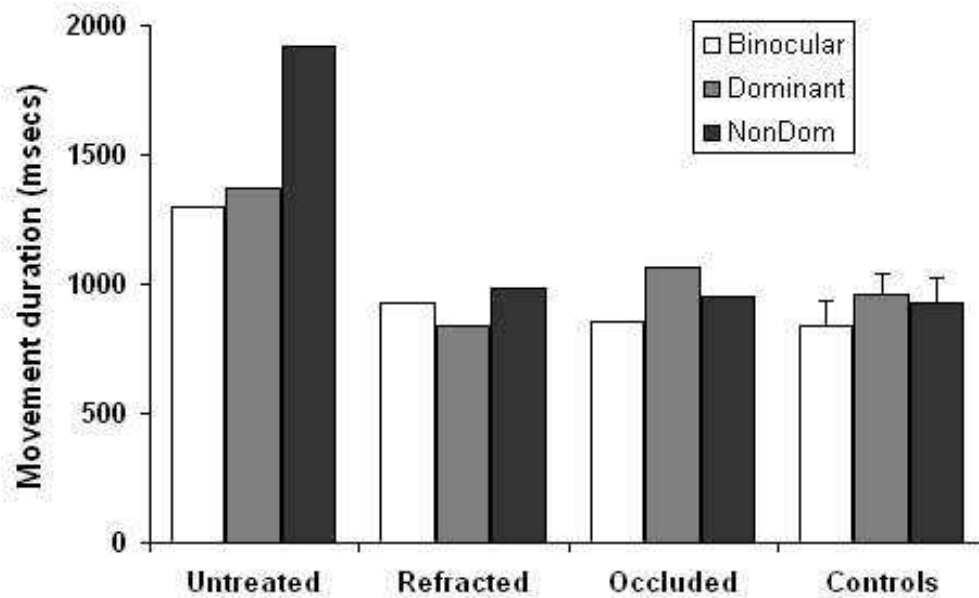


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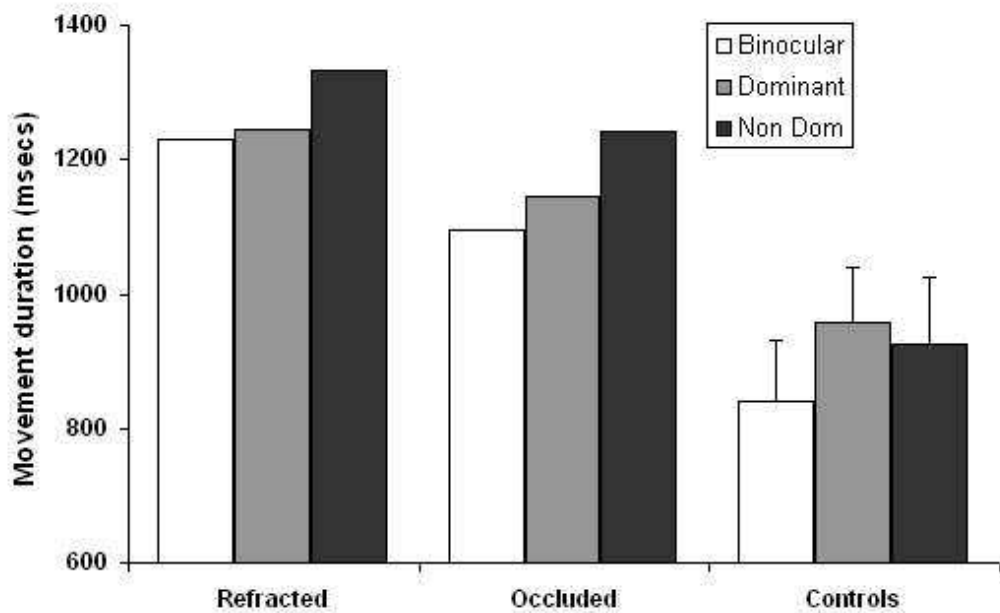


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Table 1: Summary of patient details

Patient Status		Ages 5-6 (n=30)	Ages 7-9 (n=25)
Visual Acuity:	logMAR IOD range	0.02-1.10	0.02-1.10
	Mean IOD (\pm sd)	0.39 (\pm 0.28)	0.43 (\pm 0.28)
Amblyopia:	Cured	7	4
	Mild	12	12
	Moderate	11	9
Stereo Acuity:	Cured	1	5
	Coarse	11	9
	Nil	18	11
Treatment:	Refractive Adaptation	3	5
	Partial Occlusion	9	7
	Completed/Follow-up	18	13
Cause:	Anisometropia	8	11
	Strabismus	20	12
	Mixed	2	2

Table 2. Mean (\pm sem) hand movement kinematics by age, group and viewing condition

Dependent Measures	Group	View		
		Binocular	Dom Eye	Non-Dom Eye
Ages 5-6 years				
Movement Duration (ms)**	Control	829 (74)	911 (65) L	931 (77) L
	Patient	1075 (49)	1106 (43)	1136 (51)
Time to Peak Velocity (ms)*	Control	266 (21)	293 (19)	283 (22)
	Patient	322 (14)	336 (14)	337 (14)
Low Velocity Phase (%)**	Control	18.8 (3.7)	18.6 (3.1)	22.4 (3.7)
	Patient	32.8 (2.1)	31.0 (1.8)	32.8 (2.0)
Post-Contact Time (%)	Control	15.8 (1.2)	14.9 (1.2)	14.8 (1.5)
	Patient	15.6 (0.8)	16.0 (0.7)	15.5 (0.9)
Peak Grip Aperture (mm)*	Control	77.7 (2.1)	81.8 (2.1) B	83.0 (2.0) BB
	Patient	75.4 (1.4)	75.6 (1.4)	76.0 (1.3)
Grip Closure Time (ms)*	Control	166 (12)	197 (19) L	204 (21) L
	Patient	269 (25)	251 (20)	263 (27)
Grip Size at Contact (mm)	Control	51.7 (1.7)	58.4 (2.2) BB	60.2 (2.7) BB
	Patient	51.4 (1.1)	54.9 (1.4)	56.3 (1.8) B
Ages 7-9 years				
Movement Duration (ms)	Control	850 (41)	966 (45) BB	978 (43) BB
	Patient	915 (32)	985 (35) L	981 (33) L
Time to Peak Velocity (ms)	Control	292 (17)	292 (15)	293 (14)
	Patient	313 (13)	326 (11)	326 (11)
Low Velocity Phase (%)	Control	28.3 (2.5)	31.0 (2.9)	32.1 (2.0) L
	Patient	28.0 (2.8)	29.3 (2.0)	29.4 (2.2)
Post-Contact Time (%)*	Control	14.8 (1.1)	15.3 (1.2)	14.3 (1.2)
	Patient	17.2 (0.8)	17.5 (0.9)	17.4 (0.9)
Peak Grip Aperture (mm)	Control	74.7 (2.7)	77.7 (2.7) L	79.1 (3.1) L
	Patient	75.1 (1.8)	75.3 (2.1)	74.8 (2.4)
Grip Closure Time (ms)	Control	196 (14)	233 (21)	241 (20)
	Patient	198 (11)	219 (13)	214 (13)
Grip Size at Contact (mm)	Control	49.5 (1.3)	52.8 (1.4) L	52.3 (1.5) L
	Patient	49.2 (1.4)	51.2 (1.2)	52.4 (1.4) L

Key: Asterisks denote significant between-group differences in the given measure: * $p < 0.05$; ** $p \leq 0.01$. Letters denote significant within-group differences in Dominant (Dom) or Non-Dominant (Non-Dom) eye performance compared to binocular viewing according to *post hoc* tests: B $p < 0.05$, Bonferroni; BB $p \leq 0.01$, Bonferroni; L $p < 0.05$, Least Significant Difference

Table 3. Mean (\pm sem) movement error-rates/trial by age, group and viewing condition

Dependent Measures	Group	View		
		Binocular	Dom Eye	Non-Dom Eye
Ages 5-6 years				
Total Reach Errors*	Control	0.47 (0.10)	0.74 (0.09) BB	0.72 (0.08) BB
	Patient	0.83 (0.07)	0.91 (0.06)	0.92 (0.06)
Late Velocity corrections*	Control	0.36 (0.04)	0.46 (0.04) L	0.48 (0.03) L
	Patient	0.51 (0.05)	0.59 (0.04)	0.60 (0.05)
Object Collisions**	Control	0.06 (0.03)	0.17 (0.04) L	0.14 (0.04) L
	Patient	0.05 (0.01)	0.05 (0.01)	0.07 (0.02)
Spatial Path corrections**	Control	0.05 (0.04)	0.11 (0.05)	0.10 (0.03)
	Patient	0.27 (0.03)	0.27 (0.03)	0.26 (0.03)
Total Grasp Errors***	Control	0.47 (0.06)	0.65 (0.07)	0.73(0.10)
	Patient	1.09 (0.09)	1.13 (0.07)	1.30 (0.08) L
Pre-Contact Grip adjustments***	Control	0.02 (0.01)	0.04 (0.02)	0.05 (0.03)
	Patient	0.18 (0.03)	0.16 (0.03)	0.17 (0.03)
Post-Contact Grip adjustments**	Control	0.15 (0.04)	0.30 (0.07) L	0.35 (0.07) L
	Patient	0.50 (0.05)	0.47 (0.05)	0.55 (0.05)
Prolonged Object Contacts***	Control	0.07 (0.02)	0.06 (0.03)	0.06 (0.03)
	Patient	0.24 (0.04)	0.17 (0.03)	0.18 (0.03)
Wide Grips at Contact*	Control	0.23 (0.03)	0.25 (0.03)	0.27 (0.03)
	Patient	0.27 (0.03)	0.33 (0.03)	0.40 (0.03) BB
Ages 7-9 years				
Total Reach Errors	Control	0.45 (0.05)	0.61 (0.07)	0.74 (0.08) B
	Patient	0.62 (0.06)	0.70 (0.06)	0.76 (0.05) L
Late Velocity corrections	Control	0.30 (0.05)	0.38 (0.05)	0.47 (0.06) L
	Patient	0.38 (0.04)	0.41 (0.04)	0.46 (0.04) L
Object Collisions	Control	0.07 (0.05)	0.08 (0.03)	0.06 (0.02)
	Patient	0.04 (0.01)	0.05 (0.01)	0.07 (0.02)
Spatial Path corrections*	Control	0.08 (0.02)	0.15 (0.03) B	0.22 (0.04) BB
	Patient	0.20 (0.03)	0.25 (0.04)	0.22 (0.02)
Total Grasp Errors	Control	0.49 (0.06)	0.93 (0.08) BB	0.84 (0.10) BB
	Patient	0.84 (0.08)	0.91 (0.06)	0.95 (0.08)
Pre-Contact Grip adjustments	Control	0.05 (0.02)	0.06 (0.02)	0.10 (0.02)
	Patient	0.07 (0.02)	0.09 (0.02)	0.13 (0.03) L
Post-Contact Grip adjustments	Control	0.22 (0.04)	0.53 (0.07) BB	0.43 (0.08) BB
	Patient	0.34 (0.04)	0.35 (0.05)	0.32 (0.04)
Prolonged Object Contacts**	Control	0.06 (0.02)	0.06 (0.02)	0.09 (0.02)
	Patient	0.19 (0.03)	0.18 (0.03)	0.17 (0.02)
Wide Grips at Contact	Control	0.16 (0.02)	0.28 (0.03) BB	0.22 (0.03)
	Patient	0.24 (0.04)	0.29 (0.03)	0.33 (0.03) L

Key: Conventions as in Table 2, except: between-group differences, *** $p \leq 0.001$

Table 4. Reach-to-grasp performance of the longitudinal cases compared to age-matched controls

Subjects	Age	IOD, SA	Move Times			Reach Errors			Grasp Errors		
			Bino	Dom	NonD	Bino	Dom	NonD	Bino	Dom	NonD
Px A1											
Untreated	7.75	1.88, NIL	✓	✓	✓	✓	✓	✓	✓		✓
Refracted	8.0	0.78, 100	✓			✓			✓		
Occluded	8.75	0.52, 60									
Px A2											
Untreated	7.33	0.88, 300	✓	✓	✓	✓	✓		✓	✓	
Refracted	7.8	0.44, 170							✓	✓	
Occluded	8.2	0.30, 100							✓		
Px M1											
Refracted	6.1	0.62, NIL	✓	✓		✓	✓	✓	✓		✓
Occluded	7.1	0.34, NIL	✓	✓	✓	✓	✓	✓	✓		
Px S1											
Refracted	7.0	0.40, NIL	✓	✓	✓	✓	✓	✓	✓	✓	✓
Occluded	7.5	0.14, NIL	✓	✓		✓	✓		✓		✓

KEY: IOD, logMAR interocular acuity difference; SA, stereoacuity in arc secs; NIL, unmeasurable; Move Times; total movement durations; Bino; binocular; Dom, dominant eye; NonD, non-dominant eye. ✓, data obtained for the given parameter was above the upper 95% confidence limit of the matched controls. Px, patient; Untreated, tested prior to spectacle wear; Refracted, tested after 3-4 months optical correction; Occluded, tested immediately after patching therapy or at 3-6 months follow-up.

Table 5. Movement deficits by age, view, visual acuity and stereovision loss

Dependent Measures: Ages 5-6 years	Binocular Vision				Dominant Eye				Non-Dominant Eye			
	Mild	Mod	S+	S-	Mild	Mod	S+	S-	Mild	Mod	S+	S-
Movement Durations		*√		√		√		√		√		√
Grip Closure Times		√		√		*√				√		
Late Velocity corrections	√	√		√								
Spatial Path corrections	√	√		√	√	√		*√	√	√		*√
Pre-Contact Grip adjustments	√	√		√				√				√
Post-Contact Grip adjustments	√	√		√	√			√		√		√
Prolonged Object Contacts	√		√	√		√		√	√			√
Wide Grips at Contact												√
N=	5	6	1	7	2	4	0	5	2	4	0	6
Dependent Measures: Ages 7-9 years	Binocular Vision				Dominant Eye				Non-Dominant Eye			
	Mild	Mod	S+	S-	Mild	Mod	S+	S-	Mild	Mod	S+	S-
Spatial Path corrections		√		*√								
Prolonged Object Contacts		√	√	√		√		√		√		
Wide Grips at Contact				√					√			√
N=	0	2	1	3	0	1	0	1	1	1	0	1

Key: Mod = Moderate amblyopia; S+ = Stereo+; S- = Stereo Nil; √ = significantly different from age-matched control subjects (Bonferroni corrected); * = significant difference between the two patient categories (Bonferroni corrected)