

# Fine Motor Skills of Children With Amblyopia Improve Following Binocular Treatment

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**PURPOSE.** The purpose of this study was to determine whether reduced fine motor skills in children with amblyopia improve after binocular treatment and whether improvements are sustained once treatment has ceased.

**METHODS.** Fine motor skills (FMS [Bruininks-Oseretsky Test of Motor Proficiency]), visual acuity (VA [Early Treatment of Diabetic Retinopathy Study chart]) and level of binocular function (BF [Randot preschool stereoacuity and Worth 4 Dot]) were measured in children with amblyopia ( $n = 20$ ; age:  $8.5 \pm 1.3$  years; 11 anisometric; 5 strabismic; 4 mixed) and in a group of visually normal children ( $n = 10$ ; age:  $9.63 \pm 1.6$  years). Eighteen children with amblyopia subsequently completed 5 weeks of binocular treatment provided by home-based dichoptic iPod game play. FMS, VA, and BF were retested at the end of treatment and 12 weeks after treatment cessation. All visually normal children also completed FMS measurements at baseline and 5 weeks later to assess test-retest variability of the FMS scores.

**RESULTS.** Prior to treatment, FMS scores in children with amblyopia were poorer than those in children with normal vision ( $P < 0.05$ ). In the children with amblyopia, binocular treatment significantly improved FMS scores ( $P < 0.05$ ). Better baseline amblyopic eye VA and BF were associated with greater improvements in FMS score. Improvements were still evident at 12 weeks post treatment. In the visually normal children, FMS scores remained stable across the two test sessions.

**CONCLUSIONS.** Binocular treatment provided by dichoptic iPod game play improved FMS performance in children with amblyopia, particularly in those with less severe amblyopia. Improvements were maintained at 3 months following cessation of treatment.

**Keywords:** amblyopia treatment, binocular vision, fine motor skills, stereopsis, strabismus

Amblyopia, a neurodevelopmental visual disorder that affects approximately 3% of the population, is associated with reduced visual acuity (VA) and degraded binocular vision, including suppression and impaired stereoscopic depth perception. Significant functional and quality of life consequences are also reported in cases of amblyopia,<sup>1–3</sup> with impairment in visuomotor control under habitual binocular viewing conditions being an important functional burden of the condition.<sup>4–8</sup> Larger fine motor skill (FMS) deficits have been associated with worse amblyopic eye VA and stereopsis,<sup>7,9–13</sup> suggesting that motor defects may be secondary to the visual impairments resulting from amblyopia. However, poorer performance in motor skills tasks has also been attributed to the underlying abnormal neural development of amblyopia.<sup>4</sup>

Although a limited number of studies have reported that the vision impairments associated with amblyopia have an impact on everyday visuomotor activities and may limit career choices,<sup>2</sup> whether successful treatment reduces the functional burden of amblyopia has yet to be established.<sup>14</sup> Numerous studies report the change in acuity and binocular vision following amblyopia treatment, but it is not known whether treatment also improves visuomotor function.<sup>2</sup> An association between improved stereovision following occlusion therapy and reach-to-grasp performance has been reported in a small ( $n$

$= 4$ ) pilot experiment<sup>7</sup>; however, most amblyopia treatment studies have not included motor function as an outcome measure.

Currently, amblyopia is treated over an extended period of many months by patching the fellow eye to force use of the amblyopic eye for 2 to 6 hours per day or by penalizing the fellow eye with atropine eye drops (which blur vision) for several days a week.<sup>15,16</sup> However, although current treatments significantly improve VA, there are issues with compliance, psychosocial side effects,<sup>17,18</sup> and regression.<sup>19</sup> Furthermore, many patients are left with residual amblyopia despite prolonged therapy.<sup>20</sup> Recently, a new approach to the treatment of amblyopia that targets binocular visual function has been reported.<sup>20–25</sup> The treatment is designed to reduce suppression through repeated activities that require simultaneous binocular perception and aims to improve stereopsis and amblyopic eye VA. Simultaneous perception is achieved by presenting a subset of stimulus elements to the amblyopic eye at high contrast and a separate subset of elements to the fellow eye at reduced contrast. A number of cohort studies have reported improvements in amblyopic eye VA and stereopsis in adults and children following short periods of supervised binocular treatment.<sup>21–34</sup> The treatment can now be delivered in the form of a modified video game on an iPod or iPad device



**TABLE 1.** Standardized Tasks Undertaken in FMS Assessment (Upper Limb Speed and Dexterity Item of BOTMP)<sup>36</sup>

Sub Item	Description	Record
1. Placing pennies in a box	Places pennies one at a time into an open box.	The number of pennies placed into the box correctly in 15 s.
2. Placing pennies in two boxes with both hands	Simultaneously picks up a penny with each hand and places the pennies into separate boxes. The subject is given a maximum of 50 s to place seven pairs of pennies into the boxes correctly.	The time taken to complete the task. A time of 50 s is recorded if the subject places fewer than seven pairs of pennies into the boxes correctly.
3. Sorting shape cards	Sorts a mixed deck of red and blue cards into two piles, separating them by color.	The number of cards correctly sorted in 15 s.
4. Stringing beads	Strings beads onto a shoelace.	The number of beads placed correctly in 15 s.
5. Displacing pegs	Displaces pegs with 2 mm base diameter on a pegboard, moving each peg to the hole directly above it.	The number of pegs displaced correctly in 15 s.
6. Drawing vertical lines	Draws straight lines between pairs of horizontal lines.	The number of vertical lines drawn correctly in 15 s. Accuracy following specific test guidelines.
7. Making dots in circles	Makes a pencil dot inside each of a series of circles.	The number of circles dotted correctly in 15 s.
8. Making dots	Makes pencil dots on a blank page.	The number of separate dots made in 15 s.

All tasks were done with the preferred hand, except for item 2, which requires both hands. A practice trial preceded each test run.

(Apple, Cupertino, CA, USA) for home use.<sup>25,26</sup> Home-based delivery of binocular treatment on an iPad, prescribed for 1 hour per day for up to 1 month, has been found to improve VA<sup>27</sup> and sometimes,<sup>27,29</sup> but not always,<sup>22</sup> stereopsis in previously treated patients with amblyopia.

In this study we tested the hypothesis that 5 weeks of home-based binocular treatment delivered in the form of a game using a portable iPod device for 1 hour per day would improve FMS in children with residual amblyopia. We also assessed whether any change in FMS in the amblyopia group was above the test-retest variability that might arise with repeated measurement of motor function.

## METHODS

### Participants

Children 7 to 12 years of age were identified from the first author's (AW) optometry practice or were referred from pediatric ophthalmologists. Inclusion criteria for the amblyopia group were VA in the amblyopic eye from 6/9 to 6/48 (0.2–0.9 logMAR), VA in the nonamblyopic eye of 6/7.5 (0.1 logMAR) or better, an inter-eye acuity difference of 2 or more lines (0.2 logMAR), and the presence or history of amblyogenic strabismus and/or anisometropia ( $\geq 1.00$  D difference in refractive error between eyes). Baseline measurements were made after at least 16 weeks of optical treatment (correction of refractive error) if required. All children with amblyopia had received conventional treatment prior to participating in the study. Fifteen of the children (83%) who participated in the binocular game-based treatment had undergone patching or atropine treatment in addition to any required optical treatment prior to entering the study. These children had persistent but stable VA deficits despite previous amblyopia penalization treatment. Three children had newly diagnosed amblyopia and had received approximately 4 months of optical treatment only (indicated by an asterisk in Supplementary Table).

Inclusion criteria for the comparison group were no history of previous treatment for amblyopia or an amblyogenic condition, normal VA (at least 6/7.5, 0.1 logMAR; best corrected VA in each eye) with less than 0.1 logMAR VA difference between eyes, and normal stereopsis (40 arcsec using the Randot Preschool Stereoacuity Test).<sup>35</sup>

The study was conducted in accordance with the requirements of the Queensland University of Technology Human Research Ethics Committee. All participants were given a full explanation of the experimental procedures, and written informed consent was obtained from both parent and child. The option to withdraw from the study at any time was explained to both parent and child. All protocols were in accord with the guidelines of the Declaration of Helsinki.

### Fine Motor Skills Assessment

Fine motor skills were evaluated using item 8 of the Bruininks-Oseretsky Test of Motor Proficiency (BOTMP).<sup>36</sup> This test provides a measure of motor proficiency as well as separate measurements of gross and fine motor skills. The BOTMP is designed for children 4 to 14 years of age and is standardized. Item 8, which assesses upper limb speed and dexterity, was selected based on the results of our previous study,<sup>4</sup> which showed that children with amblyopia exhibited the greatest deficit relative to controls on this test item. The upper limb speed and dexterity item (Table 1) consists of eight timed sub-items that measure hand and finger dexterity, hand speed, and arm speed. Point scores for each sub-item are derived and then summed to arrive at the raw score. Age-standardized scaled scores are calculated by referring the raw score to published normative values.<sup>36</sup>

### Vision Assessment

Monocular and binocular VA with optimal refractive correction were measured using a computerized Early Treatment of Diabetic Retinopathy Study chart<sup>37</sup> following the screening and threshold procedure used in the Amblyopia Treatment Study VA protocol.<sup>38</sup> The child was asked to read the first letter of each row from the top of the chart until an error was made (screening). The child was then redirected to two rows above the screening error row and asked to attempt to read each letter until four incorrect responses were given (threshold). VA in logMAR units was scored on a letter-by-letter basis.

Level of binocular function was assessed using the Randot Preschool Stereoacuity Test<sup>35</sup> and the Worth 4 Dot test.<sup>39</sup> The Randot Preschool Stereoacuity test was administered and scored according to the manufacturer's instructions. Stereoacuity was recorded as log arc second of the smallest disparity target that the child was able to correctly identify. The Worth 4 Dot test was used to indicate the presence or absence of

binocularity in those who had no measurable stereoacuity. The child reported the number and color of the lights seen, tested at both 6 m (1° lights) and 33 cm (6° lights). If stereopsis was not measurable on the Randot test but the child did not suppress on the Worth 4 Dot test (i.e., they reported four lights), a log threshold of 4 was recorded.<sup>27</sup> If the child reported only 2 red or 3 green lights on the Worth 4 Dot, they were considered to have complete suppression (assigned a log threshold score of 5). Assigning a value to represent the presence or absence of suppression in this way enabled inclusion of all participants in the analysis of binocular function as an extension of the stereoacuity scale.

### Amblyopia Treatment: iPod Dichoptic Game-Play

The children with amblyopia played a modified version of the videogame Tetris (Nintendo, Kyoto, Japan) on a study iPod that was loaned to them (iPod Touch fifth generation model; screen size 4 inches). The game required the child to manipulate the position and rotation of falling blocks to tessellate them with base blocks. This game has been used in previous binocular game-play amblyopia treatment studies.<sup>22,25,27</sup> Red and green filters were worn while viewing the iPod to enable dichoptic presentation of the blocks. Red falling blocks at 100% contrast were visible to the amblyopic eye; the top two rows of stationary green base blocks, presented at reduced contrast, were visible to the fellow eye; and the remaining base blocks were visible to both eyes. Amblyopic eye contrast was set to 100%. The fellow eye contrast was set at 15% to 20% based on the child's ability to successfully play the game during a training session that was part of the baseline visit.

The game had a constant criterion score that indicated successful game play. If the child achieved the criterion score, the contrast of the green blocks (visible to the fellow eye) was automatically increased by 10% of the previous value (e.g., 20%–22%) the next day. If the criterion score was not achieved, fellow eye contrast was reduced by 10% of the previous value on the next day. Time spent on game play was logged on the iPod device for compliance monitoring. During the baseline session, the patients and their parents were familiarized with the operation of the game and with the red-green glasses, which were worn over any habitual refractive correction. Participants were provided with a study iPod with the game installed, red-green glasses, and written instructions on how to play the game, to take home. They were instructed to play the game for 1 hour per day, which could be completed in daily sessions of 1 × 1 hour, 2 × 30 minutes, or 3 × 20 minutes 5 days per week for 5 weeks (full compliance would be 25 hours of play). The examiner contacted participants after 2 weeks to encourage compliance. Log files that recorded time engaged in game play were downloaded when the 5 weeks of treatment ceased.

### Study Design

The children with amblyopia completed tests of FMS, VA, and binocular function at baseline and following 5 weeks of home-based binocular treatment. At the 5-week visit, the study iPod was retrieved and treatment ceased. FMS, VA, and binocular function were again measured at 17 weeks following the baseline visit (3 months after treatment ceased) to test for regression of any treatment effects. The 5-week treatment time and 17-week follow-up were chosen to match time-lines that have been used in other amblyopia treatment trials in children 7 to 12 years of age.<sup>40</sup>

The visually normal children completed tests of VA, binocular function, and FMS at baseline and returned 5 weeks later for retesting of VA, binocular function, and FMS to allow

calculation of the 95% confidence interval (CI) for change. This allowed for an assessment of any practice effects induced by repeated testing.

A single examiner, who was not masked to participant group, collected all FMS and vision data. The examiner strictly adhered to published criteria for test administration and conformed to the objective scoring according to the BOTMP manual; the examiner also followed strict clinical data collection protocols for vision measurements.

### Statistical Analysis

Independent sample *t*-tests were used to compare baseline FMS scores and VA of the poorer eye between the amblyopia and comparison groups. Paired *t*-tests were used to compare FMS scores and VA at baseline versus post 5-weeks treatment (treatment effect) and post 5-weeks and post 12-weeks treatment (effect endurance) in the children with amblyopia who completed the binocular treatment. The 95% CI for the difference in means of FMS scores and VA measured at baseline and at 5 weeks post baseline were calculated for the comparison group with normal vision. In addition, mixed ANOVA with factors of time (baseline versus post 5 weeks) and group (amblyopia group versus comparison group) conducted using the scaled FMS and VA scores were used to compare the treatment effect in the amblyopia group to test and re-test changes in the comparison group with normal vision. Effect sizes were calculated using point-biserial correlations (*r*). Nonparametric tests were used to analyze the ordinal binocular function scores (Mann-Whitney *U* and chi-squared tests). Correlation coefficients were calculated to quantify the relationships between FMS scores and measurements of VA and binocular function, both at baseline and following treatment.

### RESULTS

Twenty children with amblyopia (8.5 ± 1.3 years of age) and 10 children with normal vision (9.6 ± 1.6 years of age) participated in the study. The differences in age between the groups were not statistically significant ( $t_{(28)} = -1.85$ ;  $P = 0.084$ ;  $r = 0.33$ ). The clinical characteristics of the participants with amblyopia are shown in the Supplementary Table. Two children (Supplementary Table, participants 15 and 17) completed baseline measurements but withdrew from the treatment study after 2 weeks, citing boredom with the game. Both children had mild amblyopia with good stereopsis at baseline.

### FMS Scores in Children With and Without Amblyopia

Baseline fine motor skills were significantly lower in the amblyopia group ( $n = 20$ ) than in the comparison group with normal vision ( $n = 10$ ), both in terms of raw score ( $t_{(28)} = -4.50$ ;  $P < 0.001$ ;  $r = 0.65$ ) and age-standardized scaled score ( $t_{(28)} = -2.46$ ;  $P = 0.020$ ;  $r = 0.42$ ). Significant differences between the groups were also found in the VA of the poorer eye ( $t_{(28)} = 11.47$ ;  $P < 0.001$ ;  $r = 0.91$ ), binocular VA ( $t_{(28)} = 5.44$ ;  $P < 0.001$ ;  $r = 0.72$ ), and binocular function score ( $Z = -4.51$ ;  $P < 0.001$ ;  $r = 0.85$ ). Table 2 summarizes mean baseline measurements for both groups. Baseline VA in the amblyopic eye and baseline binocular function were significantly correlated ( $\rho = 0.802$ ;  $P < 0.001$ ), however baseline FMS score did not significantly correlate with either amblyopic eye VA ( $r = 0.079$ ;  $P = 0.742$ ), binocular VA ( $r = 0.226$ ;  $P = 0.338$ ), or baseline binocular function score ( $\rho = 0.267$ ;  $P = 0.255$ ).

**TABLE 2.** Mean ( $\pm$  SD) Ages, FMS Scores, and Vision at Baseline for Amblyopia and Comparison Group

Outcomes	Amblyopia	Comparison Group
	Age 8.52 ( $\pm$ 1.29) y*	Age 9.63 ( $\pm$ 1.64) y†
FMS raw score	35.80 (4.53)	43.80 (4.97)
FMS scaled score (age-adjusted)	14.10 (3.37)	17.70 (4.52)
VA worse eye (logMAR)	0.44 (0.17)	-0.09 (0.08)
VA both eyes	-0.03 (0.09)	-0.21 (0.09)
BF score (log stereoacuity)	3.27 (1.31)	1.60 (0.00)

\* Amblyopia group:  $n = 20$ ; 55% female.† Comparison group:  $n = 10$ ; 40% female.

Thus, for the amblyopia group baseline, FMS score did not correlate with the severity of amblyopia.

### Effect of Binocular Treatment

FMS were retested in the 18 children with amblyopia (9 anisometric, 9 strabismic) who completed 5 weeks of home-based binocular treatment. The number of hours of play recorded on the iPod log files varied from 3 to 27 hours (mean: 11.7 hours). FMS, VA, and binocular function were retested in all the comparison children ( $n = 10$ ) following a 5-week interval to determine test-retest variability for each of the measurements. Table 3 reports mean ( $\pm$ SD) FMS scores, VA and binocular function scores for all visits for both groups.

FMS scores of the children with amblyopia significantly improved following 5 weeks of treatment both in terms of raw score ( $t_{(17)} = 7.355$ ;  $P < 0.001$ ;  $r = 0.87$ ) and age-standardized (scaled) score ( $t_{(17)} = 7.498$ ;  $P < 0.001$ ;  $r = 0.88$ ) (Fig. 1A). The improvement in FMS scaled score (mean change =  $4.17 \pm 2.36$ ; 95% CI: 2.99-5.34;  $t_{(17)} = 7.498$ ;  $P < 0.001$ ;  $r = 0.88$ ) was larger than the upper 95% CI for scaled FMS score test-retest variability in the comparison group with normal vision (mean change = 0.10; 95% CI: -1.63 to 1.83;  $t_{(9)} = 0.130$ ;  $P = 0.899$ ;  $r = 0.04$ ) (Table 3). Figure 1B shows the individual pretreatment to post treatment FMS scores for the amblyopia group; Figure 1C shows the test-retest of scores in the comparison group with normal vision. Furthermore, ANOVA revealed a significant interaction between time and group ( $F_{(1,26)} = 18.753$ ;  $P < 0.001$ ;  $r = 0.65$ ), indicating that the improvement in FMS score post treatment in the amblyopia group was significantly greater than the change in FMS score due to test-retest variability in the comparison group with normal vision. Scaled FMS scores did not differ significantly between the amblyopia and comparison groups at the 5-week time point ( $t_{(26)} = 0.452$ ;  $P = 0.7$ ;  $r = 0.09$ ).

Small but significant improvements in amblyopic eye VA were also observed after treatment (mean improvement of  $-0.09$  logMAR  $\pm$  0.10; 95% CI: -0.13 to -0.04;  $t_{(17)} = -3.725$ ;  $P$

= 0.002;  $r = 0.67$ ) (Fig. 2A; Table 3). However this improvement did not exceed the upper 95% CI for test-retest variability observed in the comparison group (mean improvement of  $-0.07 \pm 0.05$ ; 95% CI: -0.11 to -0.04;  $t_{(9)} = -4.640$ ;  $P = 0.001$ ;  $r = 0.84$ ). ANOVA revealed no significant interaction between time and group for the VA results ( $F_{(1,26)} = 0.145$ ;  $P = 0.71$ ;  $r = 0.07$ ). Figure 2B shows the individual pretreatment to post treatment VA results for the amblyopia group and the 95% CI for change for the comparison group. Six patients showed improvements in VA that exceeded the 95% CI for test-retest variability, five of whom had plateaued with patching and/or atropine and had stable VA prior to the binocular treatment (Fig. 2B).

Binocular function score (log arcsec of stereoacuity measurement with values of 4 and 5 assigned for those with simultaneous perception and suppression, respectively) changed following treatment (mean improvement of  $-0.56 \pm 0.14$ ; 95% CI: -0.85 to -0.27;  $Z = -3.072$ ;  $P = 0.002$ ;  $r = 0.75$ ) (Table 3; Figs. 3A, 3B). The proportion of children with amblyopia at different levels of binocular function changed following treatment ( $\chi^2 = 12.400$ ;  $P = 0.015$ ;  $r = 0.82$ ). Specifically, at baseline, 6 children were suppressing their amblyopic eye (41%), 2 had simultaneous perception as measured on the Worth 4 dot test (18%), and 10 had measurable stereoacuity (41%). At the post treatment 5-week visit, only 1 child was still suppressing, 5 had simultaneous perception (53%), and 12 had stereoacuity (47%). Eight of the children with amblyopia (47%) improved 1 level of binocular function; one child improved 2 levels (from suppression to measurable stereoacuity). All participants within the comparison group were at ceiling for binocular function score as this was an inclusion criterion for the comparison group.

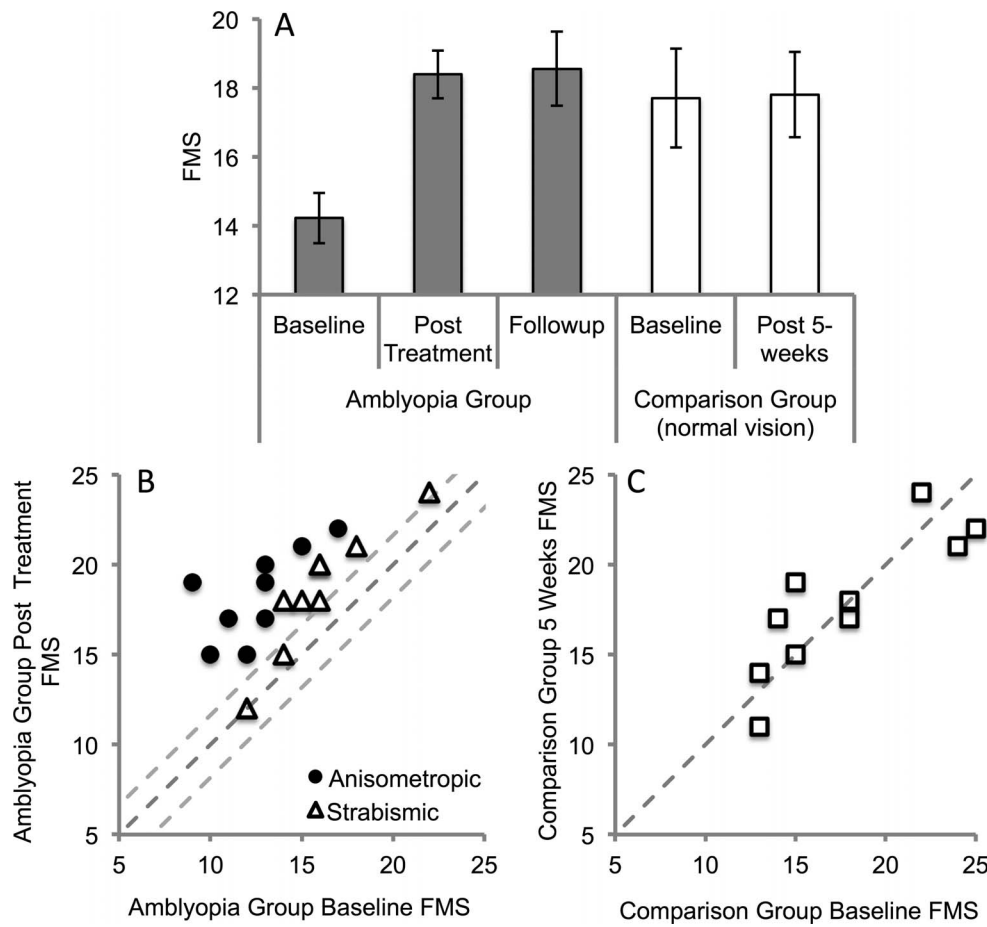
### Correlations Between FMS Outcome Following Treatment and Vision Measurements

The change in FMS scaled score following treatment was significantly correlated with baseline binocular function score ( $\rho = -0.754$ ;  $P < 0.001$ ) (Fig. 4A) and baseline VA ( $r = -0.639$ ;  $P = 0.004$ ) (Fig. 4B), where the higher the level of baseline VA and the better the initial binocular function the greater the improvement in FMS scaled scores. In this sample, the patients who exhibited the largest improvement in FMS with treatment tended to have anisometric rather than strabismic amblyopia (Fig. 1B). The degree of change in FMS score following treatment did not significantly correlate with the change in binocular function ( $\rho = 0.121$ ;  $P = 0.632$ ) or change in VA ( $r = 0.356$ ;  $P = 0.147$ ) induced by treatment, nor did it correlate with the number of treatment hours recorded on iPod log files ( $r = -0.010$ ;  $P = 0.968$ ) (Supplementary Table, completed training hours).

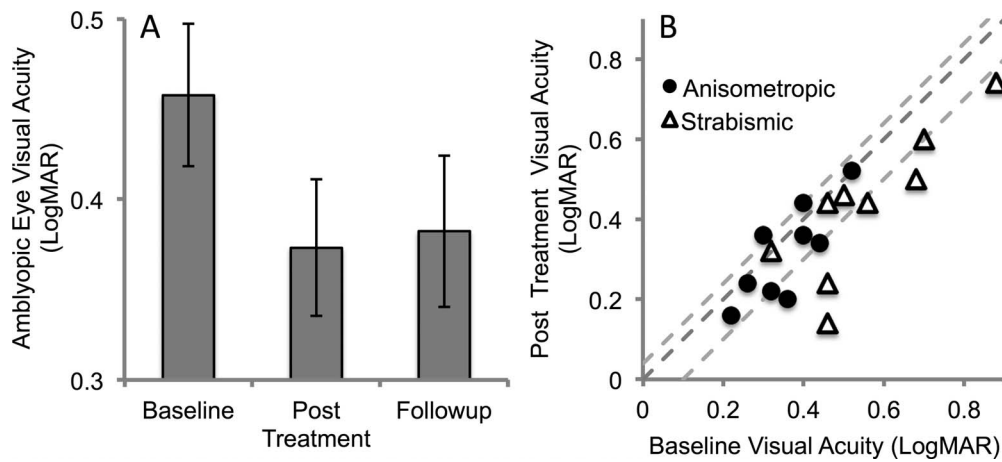
**TABLE 3.** Mean ( $\pm$  SD) FMS Scores and VA and BF at Baseline and Following 5-Weeks Amblyopia Treatment

Outcomes	Treated Amblyopes Age 8.52 ( $\pm$ 1.25) y*			Comparison Group Age 9.63 ( $\pm$ 1.64) y†	
	Baseline	5 wk (Post Treatment)	17 wk (12 wk After Treatment Ceased)	Baseline	5 wk (Test-Retest Variability)
FMS raw score	35.94 (4.76)	40.72 (4.43)	42.28 (5.34)	43.80 (4.73)	43.90 (5.20)
FMS scaled score	14.22 (3.10)	18.39 (2.93)	18.56 (4.38)	17.70 (4.52)	17.80 (3.91)
VA worst eye (logMAR)	0.46 (0.16)	0.37 (0.16)	0.36 (0.18)	-0.09 (0.08)	-0.16 (0.09)
VA both eyes (logMAR)	-0.03 (0.09)	-0.06 (0.09)	-0.03 (0.06)	-0.21 (0.09)	-0.20 (0.08)
BF score (log stereoacuity)	3.44 (1.27)	2.88 (1.05)	2.74 (1.06)	1.6 (0.0)	1.6 (0.0)

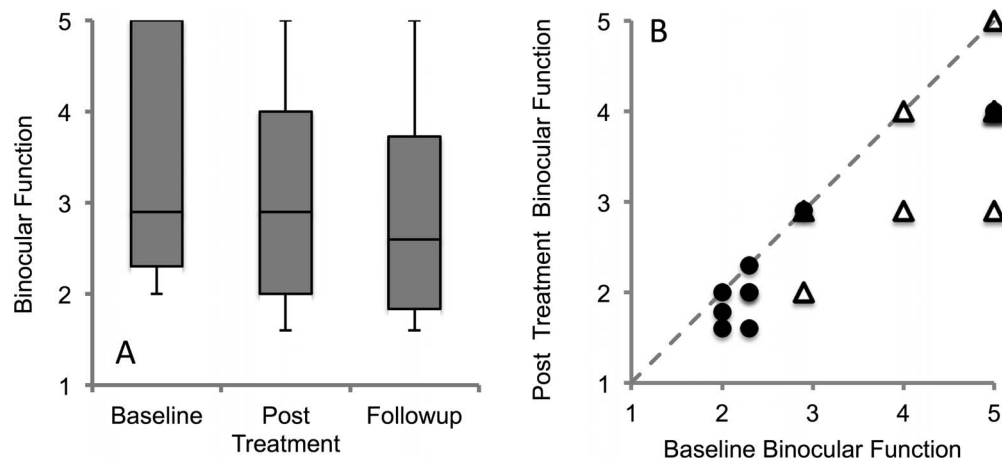
\* Treated amblyopes:  $n = 18$ ; 55% female.† Comparison group:  $n = 10$ ; 40% female.



**FIGURE 1.** Changes in FMS standard scores. (A) Filled bars show amblyopia group mean FMS scores before (baseline), directly after (post treatment), and 3 months after (follow-up) treatment. Open bars show mean data for the comparison group with normal vision at baseline and 5 weeks later (post 5 weeks). Error bars show  $\pm 1$  SEM. (B) Individual data for the amblyopia group. The dashed lines on either side of the unity line indicate 95% confidence intervals 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.



**FIGURE 2.** Changes in amblyopic eye visual acuity. (A) Mean FMS scores before (baseline), directly after (post treatment), and 3 months after (follow-up) treatment for the amblyopia group. Error bars show  $\pm 1$  SEM. (B) Individual data for the amblyopia group with 95% confidence intervals for change from the comparison group with normal vision (light dashed lines). Data points falling below the lower dashed line represent changes in visual acuity that exceeded test-retest variability.



**FIGURE 3.** Changes in binocular function. Larger binocular function scores indicate worse binocular function (see text for details). (A) Medians and interquartile ranges for the amblyopia group before (baseline), directly after (post treatment), and 3 months after (follow-up) treatment. (B) Individual data.

### Persistence of Treatment Effect

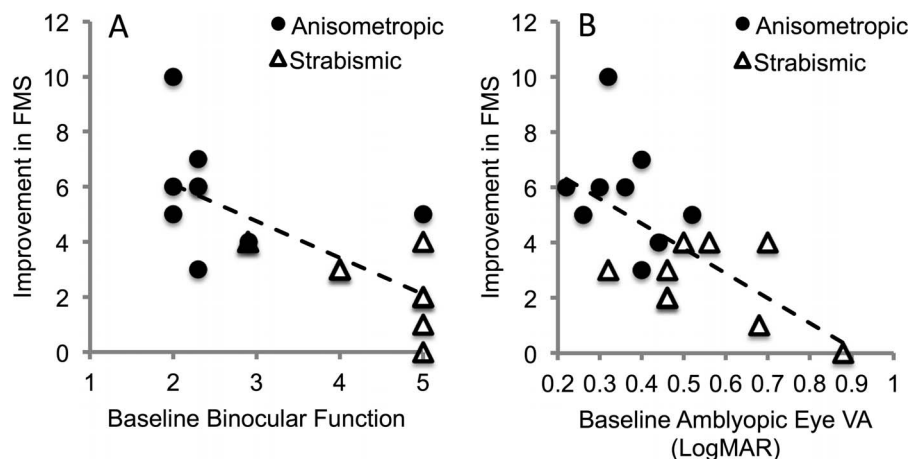
The improvements in FMS, VA, and binocular function remained at 12 weeks after treatment cessation (17 weeks post baseline) (Table 3; Figs. 1A, 2A, 3A). The mean change in FMS scaled score from ceasing treatment to review for regression was  $0.17 \pm 3.09$  (95% CI:  $-1.37$  to  $2.58$ ;  $t_{(17)} = 0.229$ ;  $P = 0.822$ ;  $r = 0.06$ ), mean change in VA was  $-0.01 \pm 0.06$  (95% CI:  $-0.04$  to  $0.02$ ;  $t_{(17)} = -0.634$ ;  $P = 0.535$ ;  $r = 0.15$ ) and mean change in binocular function score was  $-0.15 \pm 0.66$  (95% CI:  $-0.47$  to  $0.18$ ;  $Z = -0.868$ ;  $P = 0.386$ ;  $r = 0.21$ ).

### DISCUSSION

This study demonstrated that 5 weeks of home-based binocular treatment improved FMS in children with residual amblyopia and that any change in FMS was above the test-retest variability that might arise with repeated measurement. These improvements were sustained for a 3-month period post training. The likelihood of improvement in FMS score was greatest for those with better baseline acuity and binocular function, which in this sample corresponded to children with anisometric rather than strabismic amblyopia.

No previous studies have prospectively investigated the effect of treatment on functional measurements, despite growing evidence that children with amblyopia have worse motor skills than children with normal vision.<sup>5-7</sup> In agreement with our previous report,<sup>4</sup> the baseline scores of children with amblyopia were poorer than those of children without amblyopia on an age-appropriate standardized test of motor proficiency that predominantly consisted of timed manual-dexterity tasks. This finding confirms the detrimental effect of amblyopia on real-world visuomotor skills that are critical for everyday activities such as reaching and grasping, drawing, writing and manual dexterity tasks.<sup>4,5,7,13</sup> Lack of correlation between FMS scores and severity of amblyopia, as defined by amblyopic eye VA or level of binocular function, concurs with our previous finding reported for a larger sample of children with amblyopia from varied causes.<sup>4</sup> After treatment, children with amblyopia had FMS scores equivalent to those of children with normal vision. Improvement above that of the comparison group might not be expected even with continued treatment.

Binocular function improved following treatment, with restoration of simultaneous binocular perception in the majority (83%) of those who were suppressing at the baseline visit. This finding confirms reported improvements in binoc-



**FIGURE 4.** The relationship between baseline vision measurements and improvement in FMS standard scores. (A) The relationship between baseline binocular function and improvement in FMS. (B) The relationship between baseline amblyopic eye VA and improvement in FMS score. Larger y-axis values indicate a larger improvement (post-treatment FMS score [minus] baseline FMS score).

ular vision with dichoptic treatment, including a high rate of restored simultaneous binocular perception and significant improvement in stereopsis.<sup>27,29</sup> However studies that have tested binocular treatment in children have not always found a significant improvement in their measurements of binocularity.<sup>22,29,31</sup> Differences in findings may arise from the various methods of recording the level of binocular sensory fusion, differences in the causes of amblyopia in the various studies, or the supervised versus unsupervised nature of laboratory-based versus home-based treatment.

A small but significant improvement in VA (0.09 logMAR) was also evident after binocular treatment, even though most of the children with amblyopia (83%) had already reached an asymptote with conventional treatment prior to entering this study. Although the improvement is not outside the test-retest levels determined in the comparison group, the magnitude of VA change is similar to that reported in recent iPod binocular treatment studies with comparable treatment duration, in both children<sup>22,29,31</sup> and adults,<sup>27</sup> most of whom had completed conventional treatment.

FMS improved to the greatest extent in children with milder levels of amblyopia, whereas children with more severe amblyopia, particularly those with strabismus, showed little improvement in FMS score. This may have been because children with milder amblyopia were able to engage with the game in a small-screen format (an iPod touch display) more effectively than children with more severe amblyopia. Alternatively, these cases of milder amblyopia have better sensory and motor fusion and good VA in both eyes, which have been shown to facilitate accurate FMS performance in older children and young adults.<sup>41</sup>

While home-based treatment reflects clinical management of amblyopia, it is less supervised than that in a laboratory setting, and there was a considerable range recorded in the time engaged in game play by individuals, as other studies also have reported.<sup>27</sup> However, more compliance hours did not result in greater FMS improvement. The treatment group was a heterogeneous sample that included children who still had severe amblyopia, despite previous treatment. Further exploration of the underlying contributing factors to improvement in FMS requires a larger sample size and will be the subject of future studies. The lack of a dose response effect may be due to the relatively heterogeneous group of participants with amblyopia and the limited sample size that was available at a single clinical site. The question of a dose response effect needs to be explored in a large-scale study that uses fine motor skills as an outcome measure.

Considerable interest surrounds iPod-based binocular amblyopia treatment as an alternative to current treatments of patching or penalization, which have limited effectiveness in a notable proportion of children.<sup>20</sup> The iPod amblyopia treatment targets binocular dysfunction that has been suggested to be the cause of poor visuomotor skills in children with amblyopia.<sup>7,9-13</sup> A further advantage of the iPod treatment is the short training regimen (approximately 1 month). This is important for the study of treatment outcome measurements that mature rapidly in childhood such as FMS. Specifically, the impaired reaching and grasping ability of children with amblyopia improves with age,<sup>7</sup> so traditionally prescribed patching or atropine treatment regimes that can extend beyond six months introduce the likelihood that better post treatment scores were due to maturation rather than treatment. We accounted for the normal maturation in FMS by using a validated test with age-standardized scoring, and children did not progress from one standardized age band to another over the comparatively short 5-week treatment period. However, the downside of a short treatment time-frame is the potential for practice effects that can contaminate outcome measurements. To address this issue we

measured the practice effect on FMS scores in a comparison group of visually normal children. FMS scores were stable between baseline and the 5-week review appointment in the comparison group, therefore the improvement seen in the amblyopia group post treatment is unlikely to be due to practice effects or maturation and most probably reflects a real therapeutic effect. Furthermore, no significant changes in standardized scores were observed from the end of treatment to the follow-up visit in the amblyopia group. Collectively, these results indicate that normal maturation was controlled for appropriately by using age-standardized scoring of the test.

An advantage of the study methodology was the ability to quantify the difference in standardized FMS scores between the group of children with amblyopia that participated in the treatment trial and a comparison group of children with normal vision. Furthermore, 95% CI for repeated measurements of the FMS test battery could be determined so that there was clear appreciation of the level of improvement in score demonstrated in the post treatment amblyopia group. The lower CI limit for change in score in the treated group was above the upper CI limit in the comparison group. However, a limitation of the study is that an untreated control group of amblyopic children who did not play the dichoptic game was not included. Including an untreated group of children with amblyopia would further strengthen the conclusions that can be attributed to the strength of treatment. The potential for bias that a single, unmasked examiner testing all subjects could introduce was limited by strict adherence to published criteria for instructions given to the child and objective scoring according to the BOTMP manual for FMS data and established clinical data collection protocols for vision measurements.

In summary, this is the first demonstration of an improvement in standardized measure of fine motor skills involved in practical, everyday tasks following amblyopia treatment. No amblyopia treatment studies to date (including ongoing clinical trials of binocular treatment) include an outcome measurement of visuomotor control. Our findings suggest that, in addition to small but measurable improvements in VA and binocular function, game-based home treatment that targets repeated binocular experience results in improved FMS scores, particularly in patients with mild anisometropic amblyopia. Whether the improvements found in this study are specific to binocular treatment or would also occur with conventional treatment is yet to be determined. Future studies are required to further explore the functional burden of amblyopia and determine the value of treatment.

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