Perceptual Learning in Children With Infantile Nystagmus: Effects on 2D Oculomotor Behavior

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Purpose. To determine changes in oculomotor behavior after 10 sessions of perceptual learning on a letter discrimination task in children with infantile nystagmus (IN).

Methods. Children with IN (18 children with idiopathic IN and 18 with oculocutaneous albinism accompanied by IN) aged 6 to 11 years were divided into two training groups matched on diagnosis: an uncrowded training group (n = 18) and a crowded training group (n = 18). Target letters always appeared briefly (500 ms) at an eccentric location, forcing subjects to quickly redirect their gaze. Training occurred twice per week for 5 consecutive weeks (3500 trials total). Norm data and test-retest values were collected from children with normal vision (n = 11). Outcome measures were: nystagmus characteristics (amplitude, frequency, intensity, and the expanded nystagmus acuity function); fixation stability (the bivariate contour ellipse area and foveation time); and saccadic eye movements (latencies and accuracy) made during a simple saccade task and a crowded letter-identification task.

Results. After training, saccadic responses of children with IN improved on the saccade task (latencies decreased by 14 ± 4 ms and gains increased by 0.03 ± 0.01), but not on the crowded letter task. There were also no training-induced changes in nystagmus characteristics and fixation stability. Although children with normal vision had shorter latencies in the saccade task (47 ± 14 ms at baseline), test-retest changes in their saccade gains and latencies were almost equal to the training effects observed in children with IN.

Conclusions. Our results suggest that the improvement in visual performance after perceptual learning in children with IN is primarily due to improved sensory processing rather than improved two-dimensional oculomotor behavior.

Keywords: eye movements, saccadic eye movements, children’s vision, congenital nystagmus

Infantile nystagmus (IN) is characterized by the presence of rhythmic, bilateral oscillations of the eyes and is defined by its onset in the first few months of life. Infantile nystagmus may appear without an afferent visual defect, in which case it is called idiopathic IN, or with an afferent visual defect, such as albinism.1 Visual perception in children with IN is limited by oculomotor and sensory deficits.2 Shorter foveation periods, caused by the presence of involuntary oscillating eye movements, are related to poorer visual acuity (VA).2–4 In addition, sensory factors, such as foveal hypoplasia and visual deprivation, can further degrade visual acuity in subjects with IN.5,6 Interventions that successfully dampen the nystagmus generally do not result in large acuity improvements.7–9 In adults with amblyopia, visual training can improve visual performance in an impressive manner.10 Recently, we found that perceptual learning (PL), which refers to long-term changes in robust visual acuity improvements in children with IN.12 The goal here is to evaluate changes in two-dimensional (2D) oculomotor behavior after perceptual learning in this group of children.

Visual acuity of individuals with IN is severely degraded by the presence of surrounding contours or objects.13–16 Therefore, our training focused on improving visual performance under crowded circumstances. Our training also included a stringent temporal constraint; near-threshold stimuli were only presented briefly (500 ms) to the left or to the right of an initial center stimulus, and children had to redirect their gaze in order to discern the target. Saccade latencies in adults with IN are longer than in normal adult controls (0.25 vs. 0.19 seconds) when discriminating the orientations of gratings presented 3° away from fixation.17

To evaluate whether training with distractors benefitted children with IN, two training conditions were compared: a crowded condition with Landolt-Cs surrounded by distractors and an uncrowded condition with isolated Landolt-Cs. While significant distance and near visual acuity improvements were observed in both training groups, crowded near visual acuity improvements and reductions in crowding intensity were only observed in the crowded letter-training group. Possible oculomotor mechanisms that might support the observed vision improvements could be: shorter saccade reaction times, more accurate saccade landing positions, improved fixation stability, and/or longer foveation durations.

Here, we investigate training-induced changes in fixation and saccadic eye movements. Fixation stability can be quantified with the bivariate contour ellipse area (BCEA).18

The bivariate contour ellipse area is a single measure for eye
position variability within a specified time window. Individuals with central scotomas and amblyopia show enlarged BCEAs. 19–21 In subjects with IN, there is a positive correlation between saccade latency and visual acuity. 3,22 Training-induced acuity improvements might thus be related to prolonged saccade durations after training. However, latencies are also longer for individuals with IN compared with individuals with normal vision (NV). 17–23 which might explain the longer visual search times in children with IN. 24–26 Faster saccade initiation and improved landing position would particularly facilitate visual performance on tasks with time restrictions, such as our training tasks, since it would bring the target longer and closer to the center of the fovea. Both saccade latencies and accuracy are evaluated in this study.

**METHODS**

**Participants**

The current study presents eye movement data of 18 children with oculocutaneous albinism (all having IN), 18 children with idiopathic IN, and 11 age-matched children with normal vision. These children were also included in two companion papers which quantify the effect of perceptual learning on visual performance 12 and reading performance. 27 Inclusion criteria for children with IN were: age between 6 and 11 years; normal birth weight (>3000 g); birth at term (≥36 weeks); no perinatal complications and normal development; no additional impairments; and crowded distance visual acuity (DVAc) between 1.3 logMAR and 0.2 logMAR (clinical characteristics are presented in Supplementary Table S1). Children with prescription glasses wore them during measurements and training sessions.

The study was approved by the local ethics committee (CMO Arnhem-Nijmegen, The Netherlands) and conducted according to the Declaration of Helsinki.

**Ophthalmological Examination**

All children underwent an ophthalmological examination (see Ref. 12 for details) at the start of this study, and children with IN were examined again after training. In short, monocular and binocular distance visual acuity were measured at 5 m with the uncrowded and crowded version of the Landolt C-test. 6 Near vision was measured binocularly at 40 cm with the crowded and uncrowded LH version of the C-test. 22

**Fixation Stability**

The fixation task was performed binocularly at 50 cm. Children were instructed to look at a white circular dot (193.8 cd/m²) with a diameter of 1° to the best of their abilities. The stimulus was presented against a black background (0.3 cd/m²) for 31 seconds at the center of a liquid crystal display (LCD) screen. After a 5-second break, the trial was repeated. The bivariate contour ellipse area was calculated from the pooled data using the following equation:

$$A = 2 \times k \times \pi \times \sigma_H \times \sigma_V (1 - \rho^2)^{3/2},$$

where $A$ is the area of a bivariate normal ellipse, $\sigma_H$ and $\sigma_V$ are the standard deviations along the horizontal and vertical meridians, and $\rho$ is the product-moment correlation of the two position components. The value $k$ was set to 1.14, yielding 68.3% probability that a given observation falls within the ellipse area. 28

**Nystagmus Characteristics**

Nystagmus frequency was quantified by using peak analysis where only peaks with bilateral drop-offs of at least 0.5° were considered before counting a new peak. 4 Nystagmus amplitude was obtained by taking ½ of the long arm of the 95% ellipse fit ($k = 3.84$) for the data collected during the fixation task. Nystagmus intensity was calculated by multiplying nystagmus frequency with nystagmus amplitude.

The expanded nystagmus acuity function (NAFX) was used to predict the best possible visual acuity based on the assumption that no afferent deficits are present. 29 Data collected during the fixation task were used to calculate the NAFX.

**2D Saccade Task**

The saccade task was performed binocularly at 50 cm from the screen. Stimuli were white circular dots (193.8 cd/m²) with a diameter of 0.5° on a black background (0.3 cd/m²). At the start of each trial, a central fixation dot was presented for 400 to 1000 ms after which the peripheral saccade target appeared for 600 ms. Children were instructed to fixate and follow the dots as fast and accurate as possible. Targets were presented pseudorandomly at five eccentricities (2, 5, 9, 18, and 27°) and 8 directions (0:45:315°) and were presented three times, resulting in a grand total of 114 trials (4 × 8 × 3) + (1 × 6 × 3) = 114 trials. Two outcome measures were collected for the saccade task: saccade accuracy and saccade latency of primary saccades. Saccade accuracy was quantified in 2D by the amplitude gain (amplitude ratio between real and perfect saccade) and direction error (unsigned angular difference between real and perfect saccade, $|\Delta \theta|$).

**Crowded Letter Task**

In the crowded letter task, children first looked at a central stimulus patch of 7 black Landolt-Cs (0.3 cd/m²) presented against a white background (193.8 cd/m²). Then, after 500 ms, a second array of 7 Landolt-Cs appeared (for 500 ms) to the left or to the right of the initial stimulus. Children had to identify the orientation of the central target C in this second array after redirecting their gaze (Fig. 1A, right-hand panel, and Ref. 12 for details). For children with crowded DVAs >0.7 logMAR, the eccentricity of the second stimulus was 15° (viewing distance: 50 cm). For children with DVAs ≤0.7 logMAR, the eccentricity was reduced to 5° (viewing distance 130 cm) because of the limited screen dimension and pixel pitch of our monitor. Letter sizes were 0.15 logMAR above the children's uncrowded VA. Center-to-center spacing between the target and distractors varied between 1.2 and 4.0 times the letter size. Subjects also performed a single letter discrimination task, in which a central C was presented for 500 ms, and a reading task (see Refs. 12 and 27 for details).

**Training**

The crowded training task was similar to the crowded letter task described above, but target size and target-to-flanker spacing were gradually reduced as the child's performance improved. In the uncrowded training group, children worked with single Landolt-Cs (Fig. 1A, left-hand panel). Each training session consisted of 7 blocks of 50 trials. Children were trained twice per week for 5 consecutive weeks (grand total: 3500 trials). See Ref. 12 for further details about the training protocol.

**Procedure**

During pre- and posttest sessions, children were seated in front of the monitor with their head supported by a head-
After calibration of the eye tracker, they first performed the fixation and saccade task, then the single-letter and crowded-letter task, and finally the reading task. Data from the single-letter task and reading task are not included in the present report, but see Refs. 12 and 27 for results. Children with IN were measured within 2 weeks before and after training. Children with normal vision were measured twice with a 7- to 10-day interval. At retest, they only performed the saccade and letter discrimination tasks.

**Equipment**

Stimuli for the pre- and posttests were generated by a 15.6-inch laptop running a computing environment (MATLAB, version 2014b; MathWorks, Inc., Natick, MD, USA) and were presented on a 32-inch monitor (UP3214Q, 3840 × 2160 pixels; pixel pitch: 0.18 mm²; Dell, Inc., Round Rock, TX, USA). The training was executed on a 15.6-inch laptop (M3800, 3200 × 1800 pixels; pixel pitch: 0.11 mm²; Dell, Inc.). Stimulus software was written in a computing environment (MathWorks, Inc.) using program-specific functions (Psychophysics Toolbox²⁹, version 3.0.12.; MathWorks, Inc.). Stimulus events and button presses were logged with 1-ms accuracy. Eye movements were recorded in two dimensions with an eye tracking system (EyeLink 1000 Plus; SR Research Ltd., Kanata, Canada). Data were collected binocularly at 500-Hz in remote/head-free mode (resolution better than 0.05°). A chin and forehead rest was used to prevent head movements.

**Data Processing**

Preprocessing of the eye movement data entailed post hoc calibrations, drift correction, blink detection, and saccade detection. During the experiments, a drift correction was performed on a model calibration to monitor data quality during the measurements. For children with IN, a 9-point monocular calibration routine was used with the other eye occluded (details about the calibration procedure are described in the Supplementary Methods). In subjects with IN whose monocular calibration data were of poor quality and in normal controls, a post hoc calibration was performed on fixation data extracted from the saccade task. In principle, recordings from the left eye were used for analysis, but in two subjects the right eye was used because of amblyopia of the left eye (ID 29 and 36).
Blinks were detected by collecting blink messages from the eye tracking system (SR Research Ltd.), by checking accelerations ($\geq 15,000/s^2$), and by manual filtering. Manual filtering was necessary, because blink characteristics were too diverse for reliable automatic detection. Data sets were considered valid if at least 40% of the collected data was blink-free and the quality of the calibration map was satisfying (average accuracy better than 0.5°). For the crowded letter task, only data sets containing at least 10 goal directed-saccades were used.

Saccades were identified by applying the following criteria: (1) velocity on- and offset $>20^8/s$, (2) acceleration onset $>3000/s^2$ and acceleration offset $>-3000/s^2$, and (3) amplitude $\geq 0.1^8$. All saccade markings set by the detection program were visually checked by the experimenter and corrected if necessary. Primary goal-directed saccades were identified by a direction ($|\Delta \theta| < 30^8$) and amplitude criterion (gain between 0.4--1.6), and had to start within 80 to 900 ms after stimulus onset. A correction was applied for initial eye position (Fig. 1B). This coarse response-selection was needed to exclude refixations of the central stimulus, stimulus-unrelated quick-phases of the nystagmus, and possible misses in target localization due to lapses of attention and/or poor visual acuity, for example.

Foveation times were determined by applying velocity (retinal image velocity $\leq 10^8/s$) and position criteria (horizontal and vertical eye position within 2.5° around target) on the data obtained during the fixation task after blinks were removed. The position criterion was chosen after inspecting the data with OM Tools$^{22}$ and plotting calibrated data.

**Statistical Analysis**

Baseline differences between training groups and children with albinism and idiopathic IN were evaluated with univariate ANOVAs (independent variables: training group and diagnosis). Baseline differences between children with normal vision and children with IN were evaluated with independent $t$-tests. Unless diagnosis was a significant factor, data from children with albinism and idiopathic IN were pooled. Repeated measures ANOVAs were used to compare and evaluate group differences on the saccade task, because this task contained either 5 or 3 within subject levels (eccentricity and direction, respectively). Bonferroni corrections were applied for multiple comparisons. Measures of BCEA were normalized with a log$^{10}$ transformation. Training effects were evaluated by conducting a repeated measures ANOVA with training group entered as the between subjects variable and pre- and posttest as the within subject variable. Results were considered statistically significant if alpha (type I error) was $<0.05$. Unless otherwise specified, PREPOST $\times$ training group interactions were absent. In case there were interactions, post hoc paired $t$-tests were run to disentangle the interaction effects.

**RESULTS**

For 26/36 children with IN (albinism: $n = 9$; idiopathic IN: $n = 17$) and all 11/11 children with normal vision, valid eye movement recordings were collected during the fixation task and saccade task. For the crowded letter task, 17/36 recordings of children with IN could be used (albinism: $n = 6$; idiopathic IN: $n = 11$) and 9/11 of children with normal vision.

**Baseline Behavior**

There were no average baseline differences between the IN training groups on any of the fixation and saccade measures (Table 1). Only nystagmus frequency differed between children with albinism and children with idiopathic IN. Therefore, data for all but the nystagmus frequency measure were pooled across children with albinism and children with idiopathic IN.

**Nystagmus Characteristics.** In all children with IN, the direction of their nystagmus during attempted straight-ahead viewing was predominantly horizontal. Nystagmus frequency was lower for children with albinism than for children with idiopathic IN ($F(1,22) = 4.91, P = 0.037$, partial $\eta^2 = 0.18$; Fig. 2). Average nystagmus frequency was $1.5 \pm 0.3$ Hz in children with albinism and $2.7 \pm 0.4$ Hz in children with idiopathic IN. No other differences were found in nystagmus characteristics between children with albinism and idiopathic IN (Table 1).
Table 1. Overview of DVAc and Uncrowded DVA (DVAu) at Pre- and Posttest (Top Rows), and Baseline Oculomotor Measures of Children With Albinism (Alb) and Idiopathic IN in the Two Training Groups (Middle and Bottom Rows)

<table>
<thead>
<tr>
<th>Training Group</th>
<th>Uncrowded Group</th>
<th>Crowded Group</th>
<th>Differences Between Training Groups or Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Alb, n = 4</td>
<td>IIN, n = 8</td>
<td>Alb, n = 5</td>
</tr>
<tr>
<td>Age, mo</td>
<td></td>
<td></td>
<td>n.s.</td>
</tr>
<tr>
<td>DVAc before training, logMAR</td>
<td>0.45 ± 0.17</td>
<td>0.46 ± 0.20</td>
<td>0.44 ± 0.32</td>
</tr>
<tr>
<td>DVAc after training, logMAR</td>
<td>0.24 ± 0.08</td>
<td>0.34 ± 0.17</td>
<td>0.36 ± 0.29</td>
</tr>
<tr>
<td>DVAc before training, logMAR</td>
<td>0.19 ± 0.14</td>
<td>0.24 ± 0.23</td>
<td>0.29 ± 0.33</td>
</tr>
<tr>
<td>DVAc after training, logMAR</td>
<td>0.08 ± 0.17</td>
<td>0.15 ± 0.19</td>
<td>0.23 ± 0.25</td>
</tr>
<tr>
<td>Nystagmus frequency, Hz</td>
<td>1.3 ± 1.1</td>
<td>3.0 ± 1.6</td>
<td>1.6 ± 1.0</td>
</tr>
<tr>
<td>Nystagmus amplitude, deg</td>
<td>4.8 ± 4.5</td>
<td>9.0 ± 4.8</td>
<td>7.8 ± 6.9</td>
</tr>
<tr>
<td>Nystagmus intensity, deg/s</td>
<td>4.4 ± 6.8</td>
<td>13.9 ± 8.7</td>
<td>8.7 ± 11</td>
</tr>
<tr>
<td>NAFX, logMAR</td>
<td>0.16 ± 0.09</td>
<td>0.42 ± 0.21</td>
<td>0.24 ± 0.18</td>
</tr>
<tr>
<td>Fixation stability, log10 deg2</td>
<td>0.6 ± 0.5</td>
<td>1.2 ± 0.4</td>
<td>1.0 ± 0.6</td>
</tr>
<tr>
<td>Foveation time, s</td>
<td>0.22 ± 0.22</td>
<td>0.03 ± 0.02</td>
<td>0.10 ± 0.11</td>
</tr>
<tr>
<td>Saccade gain</td>
<td></td>
<td></td>
<td>n.s.</td>
</tr>
<tr>
<td>2°</td>
<td>0.73 ± 0.14</td>
<td>0.87 ± 0.24</td>
<td>0.76 ± 0.21</td>
</tr>
<tr>
<td>5°</td>
<td>0.82 ± 0.11</td>
<td>0.82 ± 0.21</td>
<td>0.75 ± 0.13</td>
</tr>
<tr>
<td>9°</td>
<td>0.91 ± 0.10</td>
<td>0.86 ± 0.15</td>
<td>0.76 ± 0.03</td>
</tr>
<tr>
<td>18°</td>
<td>0.91 ± 0.04</td>
<td>0.88 ± 0.13</td>
<td>0.86 ± 0.10</td>
</tr>
<tr>
<td>27°</td>
<td>0.87 ± 0.07</td>
<td>0.87 ± 0.16</td>
<td>0.82 ± 0.12</td>
</tr>
<tr>
<td>Saccade latency, ms</td>
<td></td>
<td></td>
<td>n.s.</td>
</tr>
<tr>
<td>2°</td>
<td>272 ± 78</td>
<td>279 ± 62</td>
<td>327 ± 110</td>
</tr>
<tr>
<td>5°</td>
<td>247 ± 27</td>
<td>258 ± 55</td>
<td>268 ± 49</td>
</tr>
<tr>
<td>9°</td>
<td>210 ± 15</td>
<td>269 ± 70</td>
<td>249 ± 50</td>
</tr>
<tr>
<td>18°</td>
<td>243 ± 18</td>
<td>287 ± 45</td>
<td>246 ± 40</td>
</tr>
<tr>
<td>27°</td>
<td>274 ± 45</td>
<td>324 ± 67</td>
<td>319 ± 98</td>
</tr>
</tbody>
</table>

n.s., not significant.

Fixation Stability. The bivariate contour ellipse areas were larger for children with IN than for children with normal vision (r(35.02) = 9.97, P < 0.001; Fig. 3, Table 2). Mean BCEA was 0.69 ± 0.12(deg)² for children with normal vision and 15.9 ± 3.1(deg)² for children with IN. Foveation times were 0.70 ± 0.17 seconds shorter in children with IN than in children with normal vision (t(11.24) = 4.24, P = 0.001, Table 2).

Saccade Accuracy and Latency on Saccade Task. Although the percentage of primary, goal-directed saccades in the saccade task was lower in children with IN compared to children with normal vision, both groups could do the task quite well (success rates 80% ± 3% and 95% ± 2%, respectively: χ²(35) = 5.01, P < 0.001). In fact, there were no significant baseline differences in saccade gain between children with IN and children with normal vision (F(1,54) = 3.29, P = 0.078, partial η² = 0.09; Fig. 4A). Mean gain was 0.91 ± 0.03 for children with normal vision and 0.85 ± 0.02 for children with IN. Eccentricity did not affect saccadic gain (values: P > 0.8, Fig. 4A). There was, however, a direction × group interaction on accuracy of saccade direction (F(2,70) = 4.55, P = 0.014, partial η² = 0.12; Fig. 5). In children with IN, the direction of horizontal saccades was more accurate (6.7 ± 0.7°) than the direction of vertical (10.5 ± 0.7°) and oblique saccades (9.4 ± 0.8°; F(2,50) = 11.74, P < 0.001, partial η² = 0.32). In children with normal vision, there was a
main effect of direction on saccade direction accuracy ($F[2,20] = 4.47$, $P = 0.025$, partial $\eta^2 = 0.31$), but pairwise comparisons between conditions were not significant. Saccade direction was on average 5.3 ± 0.9° less accurate for children with IN than children with normal vision across all directions (values: $P < 0.002$).

Saccade latencies were 47 ± 14 ms longer in children with IN than in children with normal vision ($F[1,34] = 10.67$, $P = 0.002$, partial $\eta^2 = 0.24$; Fig. 4B). Mean saccade latency was 229 ± 12 ms for children with normal vision and 276 ± 8 ms for children with IN. Eccentricity affected saccadic latencies ($F[4,136] = 14.20$, $P < 0.001$, partial $\eta^2 = 0.30$). Latencies were longer for more eccentric stimuli (Fig. 4B).

Saccade Gain and Latency on Crowded Letter Task. The percentage of saccades that were (coarsely) direct toward the target patch was higher for children with normal vision (84% ± 4%) than for children with IN (67% ± 4%) ($t[24] = 2.74$, $P = 0.013$). However, gain and latencies of the saccades that were aimed toward the target letter did not differ between children with IN and children with normal vision ($t[24] = 1.00$, $P = 0.327$, and $t[24] = 0.375$, $P = 0.711$, respectively, Table 2). Saccade latencies were on average 157 ± 20 ms longer for the crowded letter task than the saccade task for children with IN and children with normal vision ($t[25] = 7.90$, $P < 0.001$).

Table 2. Overview of Baseline Oculomotor Measures of Children With IN and Children With NV Obtained in Fixation Task (Top Rows), Saccade Task (Middle Rows) and Crowded Letter Task (Bottom Rows)

<table>
<thead>
<tr>
<th>Mean ± SD</th>
<th>IN (n = 26)</th>
<th>NV (n = 11)</th>
<th>Difference Between Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, months</td>
<td>114 ± 18</td>
<td>100 ± 16</td>
<td>$t(35) = −2.30$, $P = 0.027$</td>
</tr>
<tr>
<td>Fixation stability, log10 deg$^2$</td>
<td>1.0 ± 0.5</td>
<td>−0.2 ± 0.2</td>
<td>$t(33.02) = −9.97$, $P &lt; 0.001$</td>
</tr>
<tr>
<td>Foveation time, s</td>
<td>0.12 ± 0.20</td>
<td>0.82 ± 0.54</td>
<td>$t(11.24) = 4.24$, $P = 0.001$</td>
</tr>
<tr>
<td>Saccade gain</td>
<td></td>
<td></td>
<td>n.s.</td>
</tr>
<tr>
<td>$2^\circ$</td>
<td>0.82 ± 0.19</td>
<td>0.97 ± 0.08</td>
<td></td>
</tr>
<tr>
<td>$5^\circ$</td>
<td>0.82 ± 0.18</td>
<td>0.90 ± 0.08</td>
<td></td>
</tr>
<tr>
<td>$9^\circ$</td>
<td>0.86 ± 0.13</td>
<td>0.88 ± 0.04</td>
<td></td>
</tr>
<tr>
<td>$18^\circ$</td>
<td>0.89 ± 0.11</td>
<td>0.89 ± 0.03</td>
<td></td>
</tr>
<tr>
<td>$27^\circ$</td>
<td>0.86 ± 0.13</td>
<td>0.91 ± 0.03</td>
<td></td>
</tr>
<tr>
<td>Saccade latency, ms</td>
<td></td>
<td></td>
<td>$F(1,34) = 10.67$, $P = 0.002$</td>
</tr>
<tr>
<td>$2^\circ$</td>
<td>288 ± 76</td>
<td>222 ± 25</td>
<td></td>
</tr>
<tr>
<td>$5^\circ$</td>
<td>265 ± 47</td>
<td>205 ± 22</td>
<td></td>
</tr>
<tr>
<td>$9^\circ$</td>
<td>251 ± 53</td>
<td>210 ± 17</td>
<td></td>
</tr>
<tr>
<td>$18^\circ$</td>
<td>268 ± 33</td>
<td>233 ± 21</td>
<td></td>
</tr>
<tr>
<td>$27^\circ$</td>
<td>312 ± 69</td>
<td>275 ± 32</td>
<td></td>
</tr>
<tr>
<td>Saccade latency crowded letter task, ms</td>
<td>407 ± 81</td>
<td>445 ± 108</td>
<td>n.s.</td>
</tr>
<tr>
<td>Saccade gain crowded letter task</td>
<td>0.91 ± 0.20</td>
<td>0.94 ± 0.05</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

n.s., not significant.

Figure 4. Baseline gain and latency of saccades in IN versus NV. (A) Saccade gain at different target eccentricities. There were no significant differences between children with IN and normal vision. (B) Saccade latencies varied with eccentricity and children with IN showed longer latencies than children with NV. Error bars: ± 1 SEM.
Changes After training in Children With IN

Nystagmus Characteristics. None of the nystagmus parameters changed significantly after training regardless of diagnosis and training type (all $P$ values $> 0.3$). Average nystagmus frequency was $2.2 \pm 0.3$ Hz before training and $2.2 \pm 0.3$ Hz after training. Amplitude was $3.7 \pm 0.5$ before and $3.8 \pm 0.6$ after training. Intensity was $9.9 \pm 1.8$/second before and $10.2 \pm 2.0$/second after training. Before and after training values of the NAFX were $0.50 \pm 0.04$ and $0.50 \pm 0.03$ logMAR, respectively.

Fixation Stability. Fixation stability, as measured in the fixation task, did not change after training either (all $P$ values $> 0.7$). Bivariate contour ellipse area was $14.7 \pm 3.2$(deg)$^2$ before and $16.1 \pm 3.5$(deg)$^2$ after training. Foveation time was $0.12 \pm 0.04$ seconds before and $0.12 \pm 0.05$ seconds after training.

Saccade Accuracy and Latency on Saccade Task. Success rates on the saccade task did not differ between pretest (80% $\pm$ 5%) and posttest (84% $\pm$ 2%), but the accuracy and latency of the responses did. Saccade gains increased by $0.03 \pm 0.01$ after training ($F[1,84] = 4.81$, $P = 0.040$, partial $\eta^2 = 0.19$, Fig. 6), resulting in more accurate endpoints as the accuracy of saccade direction did not change after training ($F[1,44] = 2.10$, $P = 0.162$, partial $\eta^2 = 0.09$). Saccade latencies decreased by $14 \pm 4$ ms ($F[1,84] = 13.67$, $P = 0.001$, partial $\eta^2 = 0.39$; Fig. 7).

Saccade Gain and Latency on Crowded Letter Task. The success rate on the crowded letter task did not change after training (pre: $67\% \pm 4\%$, post: $67\% \pm 5\%$). Gains and latencies of the goal-directed responses were also unaltered ($F[1,16] = 3.10$, $P = 0.099$, partial $\eta^2 = 0.17$, and $F[1,15] = 2.86$, $P = 0.111$, partial $\eta^2 = 0.16$, respectively, Fig. 8).

Test Retest Changes in Children With Normal Vision

Saccade Accuracy and Latency on Saccade Task. The percentage of goal-directed saccades did not differ between the first and second measurement (first: 95% $\pm 2\%$, second: 95% $\pm 1\%$). Saccade gains showed a trend to be higher at the retest session (test-retest: $F[1,40] = 4.53$, $P = 0.059$, partial $\eta^2 = 0.31$; Fig. 6C) and saccade latencies tended to be shorter ($F[1,40] = 4.45$, $P = 0.061$, partial $\eta^2 = 0.31$; Fig. 7C). There was no change in accuracy of saccade direction ($F[1,20] = 2.49$, $P = 0.145$, partial $\eta^2 = 0.20$).

Saccade Gain and Latency on Crowded Letter Task. The success rate on the crowded letter task increased from the first to the second test session (first: 84% $\pm$ 4%, second: 96% $\pm$ 1%). However, neither the gain of the goal-directed responses ($F[1,8] = 1.28$, $P = 0.291$, partial $\eta^2 = 0.14$; Fig. 8A) nor their latencies ($F[1,8] = 2.92$, $P = 0.126$, partial $\eta^2 = 0.27$, Fig. 8B) were significantly altered.

DISCUSSION

The goal of the present study was to determine changes in oculomotor behavior after perceptual learning in children with IN. Baseline comparisons showed that children with IN had larger fixation instability, shorter foveation durations, lower saccade accuracy, and longer saccadic latencies than children with normal vision. We found no baseline differences in saccade gain and latency between children with IN and children with normal vision on the crowded training task. After training, saccade accuracy increased and latency of children with IN decreased in the saccade task. However, test-retest effects in children with normal vision were very similar to training effects in children with IN, indicating that the changes in oculomotor measures found in children with IN are probably not due to improved oculomotor control, but rather a consequence of being more familiar with the task.

Baseline Differences in Oculomotor Behavior

As expected, there were considerable baseline differences in fixational and saccadic eye movements between children with IN and children with normal vision. At first sight, the size of the BCEAs in our study seems smaller than the sizes reported previously in patients aged 5 to 17 years with normal vision12, but this difference is due to a different threshold-criterion for the ellipse fit (here, 68.5%). If we apply a similar 95% criterion, our results (average BCEA of 1.3 $\pm$ 0.3(deg)$^2$) match the
1.3(deg)^2 BCEA reported previously for 40 children with normal vision. Approximately one-third of the subjects with IN did not provide usable data. Young children with IN in particular were more difficult to record from, so unfortunately the age matching between children with IN and normal vision (which was present in the full subject sample, see Refs. 30, 31) did not survive in this study. Children with normal vision were 14 ± 6 months younger than children with IN. Because the accuracy of fixation eye movements might still improve and the latencies of saccades might still decrease in this age range, it is possible that the differences between children with IN and normal vision are larger if children with normal vision and IN are better matched on age.

Saccade latencies in the saccade task were 47 ± 14 ms longer in children with IN than in children with normal vision (Fig. 4B), which is in line with the 60 ms difference reported in adults. Target direction affected saccade latencies of children with IN and children with normal vision in a similar manner, suggesting that the quick phases along the horizontal axis in children with IN did not bias the latency data (Supplemental FIGURE 7.

**FIGURE 6.** Changes in saccade gains on the saccade task. Pre- and posttraining data of children with IN in the crowded training group (A) and uncrowded training group (B), and test-retest data of children with NV (C). Note small shifts toward larger saccade gains in all three panels. Data were pooled across saccade directions. Error bars: ±1 SEM.

**FIGURE 7.** Changes in saccade latencies on the saccade task. Pre- and posttraining data of children with IN in the crowded training group (A), and uncrowded training group (B). Note that there was a systematic decrease in saccade latencies after training. Test-retest data of children with NV (C) shows that children with NV also tended to be faster after performing the task once. Data were pooled across saccade directions. Error bars: ±1 SEM.
Fig. S1). Explanations for the ~160 ms longer saccadic latencies for the crowded letter task than for the simple 2D saccade task might be that there were distractors present in the crowded letter task and that the task was more difficult than the simple 2D saccade task. Surprisingly, however, saccade latencies on the crowded letter task did not differ between children with IN and children with normal vision. An explanation for this might be that in the training task, target onsets and locations were much more predictable, than in the saccade task. In addition to the difference in saccade latencies on the saccade task, we also found that saccade direction errors were 2-to 3-fold larger for children with IN (7–11°) than for children with normal vision (3–4°). In children with normal vision, there were no significant differences in the magnitude of saccade direction errors for different target directions, but there was a direction effect in children with IN. The poorer directional accuracy for vertical and diagonal saccades might be explained by the predominantly horizontal nystagmus in children with IN, which could make it more difficult to accurately program or execute the saccade’s horizontal component. Horizontal component errors were indeed larger than vertical ones (data not shown).

**Oculomotor Changes After Training**

Training did not induce changes in nystagmus characteristics or fixation eye movements. Visual performance, on the other hand, improved dramatically on the crowded letter task after training. This finding suggests that fixation stability does not necessarily have to improve for training to enhance visual performance in children with IN. It could be though that the task demand of our fixation task was too low and there was no functional gain for children to suppress or manipulate their nystagmus.

Training also had no effect on the accuracy and latency of saccades in the crowded letter task. This clearly shows that changes in saccade behavior cannot account for the better visual performance in this task either. Not only did the accuracy of crowded letter identification increase after training, subjects with IN also became 0.47 ± 0.09 seconds faster. The latter was also observed in children with normal vision (Supplementary Data and Supplementary Fig. S2). These findings show that children quickly learned to deal with the demands of the crowded letter task, but not that changes in saccade behavior truly contributed to the improved vision of children with IN. After training, children with IN showed improved performance on the saccade task, but it is difficult to attribute the improvements in saccade accuracy and latency to the training since test-retest effects in children with normal vision were quite similar. It is possible that test-retest effects in children with IN are different from those in children with normal vision (e.g., because of different learning rates). However, neither the changes in saccade accuracy nor the changes in saccade latencies were significantly correlated with any of the training-induced improvements in visual acuity (all r values ≤0.4 and all P values > 0.1; see Supplementary Data for details).

We thus conclude that the observed changes in saccade behavior cannot account for the robust improvements in visual performance after perceptual learning in children with IN. We cannot fully exclude that there were changes in binocular coordination; but taken together, our findings strongly suggest that our training paradigms primarily enhanced visual attention and/or low level sensory processing, at least on the short term. It is possible that in the longer term, the subtle improvements in oculomotor behavior do support (further) improvements in visual performance.

**Conclusions**

The 2D oculomotor behavior of children with infantile nystagmus was not significantly altered by the training. Our results therefore indicate that the effective component of
perceptual learning in children with infantile nystagmus is not primarily improved oculomotor control. Visual perception and changes in visual perception in infantile nystagmus is not solely a function of motor behavior, but can change independently of the latter. Enhanced visual attention and/or low-level sensory plasticity are much more likely to explain their visual performance improvements after perceptual learning.

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