The effect of gaze angle on visual acuity in infantile nystagmus

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Abstract

PURPOSE: Most individuals with infantile nystagmus (IN) have an idiosyncratic gaze angle at which their nystagmus intensity is minimised. Some adopt an abnormal head posture to use this ‘null zone’, and it has therefore long been assumed that this provides nystagmats with improved visual acuity (VA). However, recent studies suggest that ‘improving’ the nystagmus waveform could have little, if any, influence on VA; i.e., VA is fundamentally limited in IN. Here, we examined the impact of the null zone on VA.

METHODS: VA was measured in eight adults with IN using a psychophysical staircase procedure with reversals at three horizontal gaze angles, including the null zone.

RESULTS: As expected, changes in gaze angle affected nystagmus amplitude, frequency, foveation duration and variability of inter-cycle foveation position. Across participants, each parameter (except frequency) was significantly correlated with VA. Within any given individual, there was a small but significant improvement in VA (0.08 logMAR) at the null zone as compared with the other gaze angles tested. Despite this, no change in any of the nystagmus waveform parameters was significantly associated with changes in VA within individuals.

CONCLUSIONS: A strong relationship between VA and nystagmus characteristics exists between individuals with IN. Although significant, the improvement in VA observed within individuals at the null zone is much smaller than might be expected from the occasionally large variations in intensity and foveation dynamics (and anecdotal patient reports of improved vision), suggesting that improvement of other aspects of visual performance may also encourage use of the null zone.
Introduction

Infantile nystagmus (IN) is a regular, repetitive, predominantly horizontal involuntary movement of the eyes. It usually develops within the first six months of life, resulting in ocular oscillations that are constantly present and persist throughout life. Even in the absence of any other detectable pathology, cases of IN are typically associated with a moderate reduction in visual acuity (VA).¹

For reasons that are not fully understood, the orientation of the eye in the orbit (i.e. gaze angle) affects one or more of the characteristics of the involuntary oscillations, including the amplitude, frequency and/or waveform type.²³ This results in a direction of gaze in which the intensity of the oscillations is at a minimum, termed the null position or null zone.⁴

Individuals with IN whose null zone is not straight ahead will often adopt an abnormal head posture in order to place the eyes at this gaze angle,¹ thus dampening the nystagmus and often increasing the duration of foveations (the period in each cycle of the waveform during which the eyes move most slowly). This null zone may be used preferentially in many situations.¹ One might therefore presume that utilising the null zone would cause VA to increase. Indeed, when plotted between individuals with IN, foveation duration is positively associated with VA.⁵ Moreover, a study by Costa et al. demonstrated that the clinical VA of children with IN (as measured using the Lea Grating Acuity Test) was significantly improved by using the null zone⁶. A recent study by Proudlock et al.⁷ has found similar results, reporting that changes in gaze angle (through use of the nystagmus null zone) cause significant changes in clinically-measured VA.

In contrast to these findings, recent work has suggested that VA may be fundamentally limited in adults with IN,⁸ meaning that treatments aiming to reduce (or even eliminate)
retinal image motion associated with the eye movements are unlikely to yield large improvements to VA. This is at direct odds with the conventional view that reducing nystagmus intensity and/or increasing foveation duration will lead to improved VA. It should be remembered that, due to the retinal image motion resulting from the incessant eye movements, there is likely to be a dynamic component to the visual input in the presence of nystagmus, unlike most visual pathologies, which are ‘static’. As a result, VA (an exclusively spatial measure of the resolving power of the visual system) cannot provide a complete account of the visual experience in those with IN. Temporal factors, such as cycle-to-cycle variability in foveation position (which is known to be correlated with clinical VA between individuals$^{9,10}$), are also likely to have an impact on visual performance. In the clinic, the time taken to make a measurement of VA is not standardised. Factors specific to IN may affect how long it takes to achieve a VA threshold. This may explain why some clinical studies report a link between nystagmus characteristics and VA, whereas others do not. In studies that have measured VA using a psychophysical protocol, such as a forced choice staircase in which the participants have unlimited time to achieve their threshold resolution, modifications to the nystagmus waveform have repeatedly failed to elicit significant changes in VA.$^{11–13}$ On the other hand, therapeutic studies that measure VA using clinical letter charts frequently report changes in acuity.$^{14,15}$

Between individuals, VA is known to correlate with characteristics of the nystagmus waveform, such as foveation duration and accuracy.$^{5,16–18}$ Furthermore, several studies have investigated, in normally-sighted individuals, the relationship between VA and foveation duration in simulated nystagmus waveforms (i.e., the test stimulus is moved in such a way as to mimic nystagmus).$^{19–22}$ The data from each of these studies are presented in Figure 1,
and clearly show an exponential relationship between simulated foveation duration and VA across individuals, i.e. VA improves with foveation duration.

Figure 1: The relationship between VA and foveation duration in simulated nystagmus in normally-sighted individuals: results from four studies (reproduced with permission from Chung and Bedell [1996])

In the present study, we aimed to determine the extent to which use of the null zone (as opposed to other gaze angles) affects VA in adults with IN, using a staircase protocol. Although lengthy in duration, these psychophysical techniques provide a more accurate visual resolution threshold than standard clinical testing, due to repeated measurement and the explicit lack of time constraints. In order to achieve this, we displayed visual targets at three horizontal gaze angles (null zone and two positions away from the null, including straight-ahead) to provoke changes in the participants’ eye movements, and measured the threshold VA at each position while simultaneously recording eye movements.

Methods

Eight individuals with idiopathic IN participated in the study (three female; 20-50 years [mean age 33]). The diagnosis of IN as reported by the participant or their ophthalmologist was investigated by an optometrist using high-speed eye movement recording,
ophthalmoscopy, colour vision testing, slit-lamp examination and a detailed family history.

No participants reported being under medical treatment or having undergone previous surgery for nystagmus. Clinical VA was measured using a self-illuminated Bailey-Lovie chart; participants were given as long as they wished to view the chart, and encouraged to continue reading until at least four letters on a line were incorrectly identified. Participants with any comorbid visual pathology besides nystagmus were excluded (one participant from an original total of nine was excluded due to previous retinal detachment). The investigation was carried out in accordance with the Declaration of Helsinki; informed consent was obtained from the participants after explanation of the nature and possible consequences of the study. The Cardiff School of Optometry and Vision Sciences Research Ethics Audit Committee granted approval for this study.

Participants were fitted with a head-mounted 1000 Hz eye tracker (IRIS; Skalar Medical BV, Delft, The Netherlands) and seated at a table with a chin/headrest. The head was comfortably restrained with foam inserts placed beside the temples. A computer-controlled rotational mirror system was used to calibrate the eye tracker. The experimental equipment and calibration method have been described previously. Following calibration, the foam inserts were removed, and the null position (rounded to the nearest 5°) for each participant was determined by asking participants to view a Landolt C target presented in the centre of a 17” monitor at an optical distance of 7 m, using the head posture with which they could most easily view the target. This gave a reading from the IRIS system of orbital eye position, indicating the amount of head turn required to view the target most comfortably.

All participants were made familiar with the psychophysical staircase procedure before recording began. The foam inserts were returned to the headrest to stabilise the head, and
Participants were asked to locate the gap in a single Landolt C, using a two-alternative forced choice paradigm (gap left or gap right). The starting size optotype was 0.40 logMAR above each participant’s best clinical VA. The presentation of subsequent Landolt C targets followed a staircase procedure using a fixed step size of 0.075 logMAR, and a three-up/one-down criterion. The staircase terminated after the criteria of 80 presentations and eight reversals had been satisfied. VA was estimated as the mean of the final six reversals. Participants performed the task at three gaze positions: their null position, primary gaze and one other eccentric gaze position, chosen to represent a wide range of viewing angles. In the one participant whose null position coincided with straight-ahead, two eccentric gaze positions were used. Eye movements were recorded throughout. Gaze angles were achieved by using the computer-controlled rotational mirror system to present the stimulus at specific angles of gaze (see Figure 2).

Figure 2: A) Schematic of laboratory layout, showing relative positions of mirror system and display. B) Photograph showing participant setup.
Regression analyses of the resulting dataset were performed using SPSS for Windows. The changes to waveform characteristics (amplitude, frequency, saccade duration and variability of saccade position) elicited by varying gaze angle were compared to the change in VA obtained both across and within-participants.

### Results

Clinical details for each of the participants are presented in Table 1.

**Table 1: Clinical data for study participants**

<table>
<thead>
<tr>
<th>Participant</th>
<th>Age / Sex</th>
<th>Clinical diagnosis</th>
<th>Ocular alignment</th>
<th>Refraction</th>
<th>Clinical VA (logMAR)</th>
<th>Null angle (°)</th>
<th>Latent component</th>
<th>Waveform type</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1</td>
<td>37 / M</td>
<td>Idiopathic</td>
<td>Ortho</td>
<td>RE: +2.25/-1.25x170 LE: +0.50/-0.75x5</td>
<td>RE: 0.30 LE: 0.10 BE: 0.10</td>
<td>10° right</td>
<td>No</td>
<td>JR&lt;sub&gt;EF&lt;/sub&gt;</td>
</tr>
<tr>
<td>P2</td>
<td>37 / M</td>
<td>Idiopathic</td>
<td>LET</td>
<td>RE: +1.50/-2.50x5 LE: +2.75/-2.75x5</td>
<td>RE: 0.32 LE: 0.32 BE: 0.32</td>
<td>5° left</td>
<td>No</td>
<td>P&lt;sub&gt;FS&lt;/sub&gt;</td>
</tr>
<tr>
<td>P3</td>
<td>38 / M</td>
<td>Idiopathic</td>
<td>XT</td>
<td>RE: -1.00/-0.75x35 LE: -0.50/-0.25x160</td>
<td>RE: 0.50 LE: 0.44 BE: 0.46</td>
<td>15° right</td>
<td>No</td>
<td>DJL / DJR / P&lt;sub&gt;FS&lt;/sub&gt;</td>
</tr>
<tr>
<td>P4</td>
<td>33 / M</td>
<td>Idiopathic</td>
<td>Ortho</td>
<td>RE: -2.00/-2.75x180 LE: -3.00/-1.75x170</td>
<td>RE: 0.24 LE: 0.18 BE: 0.18</td>
<td>15° left</td>
<td>Yes</td>
<td>P / PC / T / JL</td>
</tr>
<tr>
<td>P5</td>
<td>24 / F</td>
<td>Idiopathic</td>
<td>Ortho</td>
<td>RE: -5.00DS LE: -5.00DS</td>
<td>RE: 0.00 LE: 0.00 BE: 0.00</td>
<td>5° left</td>
<td>No</td>
<td>J&lt;sub&gt;EF&lt;/sub&gt;</td>
</tr>
<tr>
<td>P6</td>
<td>50 / M</td>
<td>Idiopathic</td>
<td>Ortho</td>
<td>RE: -11.50/-2.00x30 LE: -10.00/-1.50x90</td>
<td>RE: 0.42 LE: 0.52 BE: 0.42</td>
<td>10° right</td>
<td>Yes</td>
<td>JL</td>
</tr>
<tr>
<td>P7</td>
<td>25 / F</td>
<td>Idiopathic</td>
<td>Ortho</td>
<td>RE: ∞ LE: ∞</td>
<td>RE: 0.40 LE: 0.30 BE: 0.30</td>
<td>Primary</td>
<td>No</td>
<td>J&lt;sub&gt;EF&lt;/sub&gt; / PC</td>
</tr>
<tr>
<td>P8</td>
<td>20 / F</td>
<td>Idiopathic</td>
<td>Ortho</td>
<td>RE: -4.25/-0.75x125 LE: -3.50/-1.50x55</td>
<td>RE: 0.22 LE: 0.32 BE: 0.12</td>
<td>10° left</td>
<td>No</td>
<td>J&lt;sub&gt;EF&lt;/sub&gt;</td>
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</table>

DJ(L), dual jerk (left); ET, esotropia; J(R)(EF), jerk (right) (with extended foveation); L, left; Ortho, orthotropia; P, pure pendular; PC, pseudocycloid; P<sub>FS</sub>, pendular with foveating saccades; R, right; T, triangular; XT, exotropia
Table 2 shows the experimental data (VA and eye movement characteristics) at each of the three gaze angles for each participant. **Foveation duration** indicates the length of time participants spend with low-velocity eye movements during each nystagmus cycle, whereas **standard deviation of foveation position** can be considered as a measure of foveation accuracy, i.e. the cycle-to-cycle repeatability of foveation position. Foveations were defined as periods lasting longer than 5 ms during which eye velocity was < 4°/s and eye position was within ±2° of the stimulus, parameters which have been used in previous studies by others, e.g. 10,26.
<table>
<thead>
<tr>
<th>Participant</th>
<th>Eye position (°)</th>
<th>VA (logMAR)</th>
<th>Amplitude (°)</th>
<th>Frequency (Hz)</th>
<th>Intensity (°/s)</th>
<th>Foveation parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Foveation duration (ms)</td>
</tr>
<tr>
<td>P1</td>
<td>+10 (Null)</td>
<td>0.056</td>
<td>2.22</td>
<td>4.50</td>
<td>9.99</td>
<td>62.29</td>
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<tr>
<td></td>
<td>0</td>
<td>0.068</td>
<td>2.68</td>
<td>4.33</td>
<td>11.61</td>
<td>46.49</td>
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<tr>
<td></td>
<td>-10</td>
<td>0.081</td>
<td>2.67</td>
<td>5.55</td>
<td>14.24</td>
<td>37.30</td>
</tr>
<tr>
<td>P2</td>
<td>-5 (Null)</td>
<td>0.219</td>
<td>1.78</td>
<td>3.50</td>
<td>6.23</td>
<td>39.37</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>0.406</td>
<td>2.37</td>
<td>3.50</td>
<td>8.30</td>
<td>22.34</td>
</tr>
<tr>
<td></td>
<td>+15</td>
<td>0.431</td>
<td>7.08</td>
<td>4.67</td>
<td>33.04</td>
<td>2.25</td>
</tr>
<tr>
<td>P3</td>
<td>+15 (Null)</td>
<td>0.306</td>
<td>0.96</td>
<td>5.83</td>
<td>5.60</td>
<td>19.18</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>0.306</td>
<td>5.67</td>
<td>3.50</td>
<td>19.85</td>
<td>21.29</td>
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<tr>
<td></td>
<td>-15</td>
<td>0.331</td>
<td>9.59</td>
<td>3.67</td>
<td>35.16</td>
<td>10.08</td>
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<tr>
<td>P4</td>
<td>-15 (Null)</td>
<td>0.094</td>
<td>1.85</td>
<td>7.00</td>
<td>12.95</td>
<td>5.60</td>
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<td></td>
<td>0</td>
<td>0.181</td>
<td>2.64</td>
<td>4.83</td>
<td>12.76</td>
<td>1.86</td>
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<tr>
<td></td>
<td>+15</td>
<td>0.231</td>
<td>5.86</td>
<td>5.83</td>
<td>34.18</td>
<td>10.03</td>
</tr>
<tr>
<td>P5</td>
<td>-5 (Null)</td>
<td>0.001</td>
<td>2.11</td>
<td>4.33</td>
<td>9.14</td>
<td>93.35</td>
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<td></td>
<td>0</td>
<td>0.080</td>
<td>2.12</td>
<td>4.50</td>
<td>9.54</td>
<td>81.62</td>
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<tr>
<td></td>
<td>+10</td>
<td>0.068</td>
<td>3.06</td>
<td>4.33</td>
<td>13.25</td>
<td>93.72</td>
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<tr>
<td>P6</td>
<td>+10 (Null)</td>
<td>0.437</td>
<td>3.11</td>
<td>4.67</td>
<td>14.51</td>
<td>29.94</td>
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<tr>
<td></td>
<td>0</td>
<td>0.462</td>
<td>3.83</td>
<td>4.83</td>
<td>18.51</td>
<td>4.24</td>
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<tr>
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<td>-10</td>
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<td>10.14</td>
<td>4.33</td>
<td>43.94</td>
<td>2.13</td>
</tr>
<tr>
<td>P7</td>
<td>0 (Null)</td>
<td>0.206</td>
<td>2.60</td>
<td>6.17</td>
<td>16.03</td>
<td>25.12</td>
</tr>
<tr>
<td></td>
<td>-5</td>
<td>0.231</td>
<td>4.38</td>
<td>6.00</td>
<td>26.28</td>
<td>12.22</td>
</tr>
<tr>
<td></td>
<td>+5</td>
<td>0.319</td>
<td>4.43</td>
<td>5.50</td>
<td>24.37</td>
<td>19.64</td>
</tr>
<tr>
<td>P8</td>
<td>-10 (Null)</td>
<td>0.056</td>
<td>2.24</td>
<td>4.17</td>
<td>9.33</td>
<td>77.34</td>
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<td></td>
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<td>4.33</td>
<td>13.09</td>
<td>51.50</td>
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<tr>
<td></td>
<td>+10</td>
<td>0.044</td>
<td>3.33</td>
<td>4.50</td>
<td>14.99</td>
<td>66.16</td>
</tr>
</tbody>
</table>

To illustrate the effects of different gaze angles on the nystagmus waveform, Figure 3 shows eye movement recordings at three gaze angles for three participants (P1, P3 and P4), representing a range of waveforms (see Table 1). The upper plot in each figure shows the nystagmus waveform in the participant’s null zone. In each case, nystagmus intensity reduces considerably in the null zone.
The relationships between VA and the properties listed in Table 2 (except intensity, which is calculated as \textit{amplitude} $\times$ \textit{frequency}) are depicted in Figure 4. Each participant is represented by a different coloured symbol.
Across-participant analysis

Grouping data from all participants, amplitude exhibited a significant linear relationship with VA ($R^2 = 0.33$, $F_{1,22} = 10.82$, $p = 0.003$). Approximately 33% of the variance in VA can be
accounted for by nystagmus amplitude. No significant correlation (linear or exponential) between VA and nystagmus frequency was evident in this group of participants. Again, grouping data from all participants, standard deviation of foveation position showed a significant linear relationship with VA ($R^2 = 0.27$, $F_{1,22} = 8.24$, $p = 0.009$; Figure 4.C). The relationship between foveation duration and VA (Figure 4.D) can be described by an exponential function with the following equation:

$$y = 0.4406e^{-0.0336x}$$

The time constant of this function is 30 ms, which is within the range of time constants previously reported by Chung and Bedell and others in studies in which normally-sighted individuals were exposed to stimuli with motion simulating nystagmus waveforms (see Figure 1). Thus, 95% of the total VA change occurred after three times the exponential time constant. Data across participants in our study indicate that maximal VA should be achieved with foveation durations of 90 ms or longer.

Conducting a regression ANOVA revealed a significant relationship between foveation duration and VA across individuals ($R^2 = 0.58$, $F_{1,22} = 30.72$, $p < 0.0001$). Indeed, nearly 60% of the variation in VA can be accounted for by foveation duration.

Within-participant analysis

In order to determine whether there was a within-participant effect of gaze angle on VA, the change in VA was plotted against the change in each parameter of the nystagmus waveform at and furthest away from the null zone. These are shown in Figure 5.
Figure 5: The change in VA and nystagmus amplitude (A), frequency (B), standard deviation of foveation position (C) and foveation duration (D) within individual participants, in and out of the preferred null zone.

Using a linear mixed model analysis, none of the five nystagmus parameters (amplitude, frequency, intensity, foveation duration or foveation position variability) showed a significant relationship with VA in the eight participants. Nonetheless, paired samples t-tests examining VA in the null zone and at the two other recorded gaze angles, i.e. away from null
and then farther from the null zone, showed statistically significant improvements in VA (0.05 logMAR: $p = 0.046$ and 0.08 logMAR: $p = 0.015$, respectively).

Discussion

For many years, potential therapeutic interventions for IN have been based on the assumption that reducing nystagmus should improve VA (such as biofeedback, surgery, drugs, etc.). The implicit assumption has been that the self-generated image motion caused by nystagmus is an important contributor to poor VA. This is especially the case for the ‘pure’ idiopath in which there is assumed to be no underlying sensory defect. Contrary to this intuition, this study has shown that changes in nystagmus intensity induced by changes in gaze direction are associated with only very small changes in VA (mean = 0.08 logMAR). Nevertheless, these changes are significant.

Our study is based on participants’ own changes in nystagmus parameters with gaze angle; that is, each participant is their own control. Other studies that are also based on within-participant comparisons have reported similarly small effects of nystagmus intensity on VA. For example, studies on biofeedback have reported changes in nystagmus intensity, but only limited improvements in VA.\textsuperscript{27,28} Inducing stress increases nystagmus intensity, but again has minimal effect on VA.\textsuperscript{11,12} McLean et al.\textsuperscript{14} showed that memantine and gabapentin can substantially reduce nystagmus intensity, but produce only small improvements in VA: 0.15 ($\pm 0.18$), 0.09 ($\pm 0.05$), and 0.04 ($\pm 0.03$) logMAR for the idiopathic group and 0.05 ($\pm 0.04$), 0.04 ($\pm 0.07$), and -0.03 ($\pm 0.05$) logMAR for the sensory defect group on memantine, gabapentin and placebo treatment, respectively. McLean et al.\textsuperscript{29} recently expanded their study to a crossover design, and found no significant change in VA, despite large significant changes to nystagmus characteristics. Dunn et al.\textsuperscript{8} argued that if nystagmus-induced motion...
blur contributed to poor VA in adults, then VA should improve if retinal smear were eliminated. By using very brief stimulus exposure times (< 1 ms), they found no such improvement relative to control participants. They concluded that the lack of improvement in VA in idiopaths may be due to an unknown underlying sensory defect or meridional amblyopia.

In stark contrast, many studies have shown a strong relationship between VA and nystagmus parameters when compared between participants. Indeed, our study highlights this difference, as seen by comparing the between-participant effects in Figure 4 to the within-participant effects in Figure 5. Clearly, there is a much wider range of nystagmus parameters across individuals than can be induced within any of the individuals in this study. Thus, one possibility is that there is an underlying relationship between the nystagmus waveform and VA (as seen in Figure 4 [a, c and d]), but that there is a limited range of nystagmus parameters available to any individual. However, we are not convinced that this is the case, as individual changes do not follow the aggregate curve closely. Nevertheless, given the large variability in the relationship between VA and foveation duration, we cannot rule out this possibility. A second possibility is that the waveform adapts to the underlying VA: those with poorer VA develop nystagmus with shorter foveation periods, and the between-participant effect is the manifestation of this adaptation across participants. Individuals, on the other hand, show little or no relationship with foveation duration, as their VA is more-or-less fixed. Since the participants in the present study were all adults (mean age 33 years), we cannot rule out the possibility that adoption of the nystagmus null zone might have a greater impact on VA in infancy than in adulthood, and that early treatment of nystagmus might have greater long-term benefits to
VA. Indeed, Felius, Stager and Jost\textsuperscript{30} have demonstrated that the benefits to VA of four-
muscle surgery are greater during the critical period of visual development.

There have been attempts to relate VA to the nystagmus waveform, such as the eXpanded
Nystagmus Acuity Function (NAFX) and many others.\textsuperscript{10,16,17,31,32} These are based on the
exponential relationship between VA and foveation duration (Figure 1). The idea is that one
can predict VA based purely on the waveform, rather than measuring VA.\textsuperscript{17} However, these
indices are based on \textit{between}-participant data, and are \textit{not} based on how an individual’s VA
changes with waveform.\textsuperscript{33} Thus, an individual’s NAFX score places the individual’s average
VA along a scale relative to other individuals’ average VA, based on the average duration of
foveation periods. As we have seen, within an individual, the relationship between VA and
foveation periods is very weak, and does not follow the exponential relationship seen
\textit{between} participants. Thus, it is not possible to predict changes in VA for a specific
individual based on changes in mean foveation duration. For these reasons, the use of these
various indices is not only inappropriate, but is also misleading and circular. It would be
interesting to examine however, in a larger cohort of participants, whether certain
waveforms might be more susceptible to gaze angle induced changes in psychophysically-
measured VA.

Dickinson has previously demonstrated that the repeatable changes in nystagmus intensity
elicited by convergence do not cause VA, or any aspect of contrast sensitivity function, to
improve.\textsuperscript{34} These data raise the intriguing question of why participants choose to use their
null zone, even to the extent of adopting head postures. As reported here, although
statistically significant, the spatial resolution benefit (on average) of aligning the null zone
with the stimulus is small; equivalent to less than a line on a standard Bailey-Lovie chart. Are
these very small VA benefits significant enough to drive participants to adopt their preferred
head posture in most visual tasks, or do other related factors such as response times or
even comfort contribute? We have previously argued that the standard clinical protocol for
measuring VA does not control for aspects of visual timing, and that this may explain why
studies that do not employ a psychophysical protocol tend to find somewhat larger VA
changes in response to nystagmus waveform modifications (since viewing times are
naturally constrained by the implicit need to ‘move on’ to the next test).\textsuperscript{6,7,33}

In accordance with previous studies, we have demonstrated a relationship between
foveation duration and VA across participants. However, within an individual, there is only a
small (yet significant) relationship between the change in any aspect of nystagmus and VA,
which is also consistent with previous studies that have measured VA using a staircase
protocol.\textsuperscript{11–13} Therefore, VA in IN would appear not to be as sensitive to changes in
nystagmus, presumably because VA is fundamentally limited, either due to amblyopia or
undetected pathology.\textsuperscript{33} This raises doubts about the usefulness of pursuing treatments that
reduce nystagmus in the hope of improving vision, at least when VA is the sole outcome
measure. Another consequence is that indirect measures of VA such as nystagmus acuity
functions (which are based on between-participant factors) are not valid for predicting
individual changes in VA. At a more fundamental level, it is not clear why patients prefer to
use their null zone, as the improvement in VA is very small, unless there are improvements
in other aspects of ‘functional vision’ such as response times. Therefore, we question the
relevance of using time-unrestricted VA as a sole outcome measure for nystagmus
interventions, and argue that new methods of visual assessment are required to more
accurately reflect the impact of real-time changes in nystagmus intensity on visual function.
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