

# Grating Visual Acuity in Infantile Nystagmus in the Absence of Image Motion

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**PURPOSE.** Infantile nystagmus (IN) consists of largely horizontal oscillations of the eyes that usually begin shortly after birth. The condition is almost always associated with lower-than-normal visual acuity (VA). This is assumed to be at least partially due to motion blur induced by the eye movements. Here, we investigated the effect of image motion on VA.

**METHODS.** Grating stimuli were presented, illuminated by either multiple tachistoscopic flashes (0.76 ms) to circumvent retinal image motion, or under constant illumination, to subjects with horizontal idiopathic IN and controls. A staircase procedure was used to estimate VA (by judging direction of tilt) under each condition. Orientation-specific effects were investigated by testing gratings oriented about both the horizontal and vertical axes.

**RESULTS.** Nystagmats had poorer VA than controls under both constant and tachistoscopic illumination. Neither group showed a significant difference in VA between illumination conditions. Nystagmats performed worse for vertically oriented gratings, even under tachistoscopic conditions ( $P < 0.01$ ), but there was no significant effect of orientation in controls.

**CONCLUSIONS.** The fact that VA was not significantly affected by either illumination condition strongly suggests that the eye movements themselves do not significantly degrade VA in adults with IN. Treatments and therapies that seek to modify and/or reduce eye movements may therefore be fundamentally limited in any improvement that can be achieved with respect to VA.

Keywords: orientation, amblyopia, tachistoscopic

Infantile nystagmus (IN) describes a regular, repetitive movement of the eyes. It usually develops within the first 6 months of life, causing ocular oscillations that are constant and persist throughout life. While many individuals with IN have a comorbid pathology of the visual pathway, approximately 30% appear not to and have been labeled as “idiopathic.”<sup>1</sup> Despite the absence of any other detectable pathology, idiopathic cases of IN are typically associated with a moderate reduction in visual acuity (VA), which has been assumed to be caused by the eye movements themselves. For example, the Nystagmus Acuity Function (NAF) and eXpanded NAF (NAFX) are outcome measures that quantify eye movement characteristics in order to predict VA.<sup>2,3</sup> Yet, it is not actually known to what extent image motion affects VA in individuals with IN.

Infantile nystagmus waveforms typically exhibit so-called foveations—periods during which the eyes move more slowly. It has been presumed that these periods exist to facilitate better VA by reducing motion blur induced by the eye movements. Nonetheless, the eyes are never truly stable for more than a few milliseconds. In normal subjects, an increase in image velocity (above 2.5 deg/s) causes a concordant reduction in VA and perceived contrast intensity, regardless of the direction of movement.<sup>4–7</sup> One previous study has examined the effects of comparable (nystagmoid) image motion on the vision of normal subjects, and found a decline in VA at velocities above 3 deg/s.<sup>8</sup> While many nystagmus waveforms contain foveation periods

with velocities below this threshold, some do not, even in subjects with idiopathic IN. Previous studies<sup>2,3,9,10</sup> have demonstrated a strong *intersubject* correlation between waveform dynamics and VA. In addition, in experiments in which normally sighted subjects are presented with image motion similar to that produced by nystagmus waveforms, VA improves as simulated foveation period duration increases.<sup>8,11–13</sup> This wealth of evidence has led to the assumption that poor waveform dynamics (i.e., brief or high-velocity foveations) reduce VA. Many clinical therapies have been predicated on this assumption.<sup>2,14,15</sup> Nonetheless, in principle, it remains possible that the reverse is true: that poor VA may result in the development of a waveform with less accurate, briefer foveations.<sup>16</sup>

Jin and colleagues<sup>17</sup> have demonstrated that a small flash of light is equally likely to be perceived at all times regardless of when it is presented during the nystagmus waveform. Furthermore, images stabilized on the retina, afterimages of bright flashes, and migraine auras are occasionally perceived as continuously moving in individuals with IN.<sup>18,19</sup> This evidence suggests that visual perception is continuous throughout the slow phases of nystagmus as well as during foveations. Chung et al.<sup>20</sup> have found that normal subjects presented with an image moving in a nystagmoid fashion have improved VA when the image is shown during the simulated foveations but hidden for the remainder of the slow phases. One might therefore

expect VA to be similarly degraded by motion blur during the entire slow phase in individuals with IN.

Here, we sought to measure VA in adults with IN in the *absence* of image motion, by using briefly flashed gratings in an otherwise dark environment. Abadi and King-Smith<sup>21</sup> have adopted a similar approach. They have determined the luminance required to detect the presence of a single line under continuous and tachistoscopic (0.2 ms) conditions; data were derived from four individuals with IN and three control subjects. Visual stimuli were presented to both groups with a brief flash of light to eliminate image motion, so that the impact of image motion on visual sensitivity could be estimated. They have found that sensitivity to a 16° long line oriented in the same axis as the nystagmus is higher than to a line oriented in the orthogonal axis, which is attributed to meridional amblyopia. However, the relationship between the tachistoscopic and continuous presentations is not discussed, and the sensitivity measure used (i.e., relative sensitivity) cannot be interpreted clinically. Therefore, we used gratings to directly measure the impact of image motion on VA.

## METHODS

Seventeen subjects with horizontal idiopathic IN volunteered for the study. First, the diagnosis of idiopathic IN as reported by the subject or by their ophthalmologist was investigated by an optometrist using high-speed eye movement recording, ophthalmoscopy, optical coherence tomography, and a detailed family history. Subjects with nystagmus showing any signs of coexisting ocular pathology other than strabismus were excluded. Following these examinations, four were excluded on the basis of eye movement recordings (one with gaze-evoked nystagmus but no nystagmus in the primary position; three with fusion maldevelopment nystagmus syndrome), two were excluded on the basis of history (achromatopsia and acquired nystagmus), one was excluded owing to iris transillumination (suggesting albinism), and one was excluded owing to having active pathology (Fuchs' endothelial dystrophy). Nine subjects with IN remained to participate in the study (three females, aged 21–69 years; mean, 43 years). Nine normally sighted individuals with no history of ocular disease were recruited (four females, aged 21–48 years; mean, 28 years). The investigation was carried out in accordance with the Declaration of Helsinki; informed consent was obtained from the subjects after explanation of the nature and possible consequences of the study. Ethical approval was granted by the Cardiff School of Optometry and Vision Sciences Human Research Ethics Committee.

First, clinical monocular VA of each eye was measured by using a self-illuminated logMAR chart at 3 m under clinical conditions. The eye with the best VA was then used as the test eye. Subjects with equal VA had their dominant eye tested, as determined by investigation of suppression using a distance Mallett unit. In the case of equidominance, the right eye was tested by default. For the test eye, habitual distance spectacle correction was worn, or refracted correction was provided if refractive error exceeded  $\pm 0.50$  diopters (mean sphere) from the habitual correction. The nontest eye was patched.

Subjects were seated 2 m in front of a 12° aperture in the center of a white cardboard mask, through which square-wave gratings were presented (Fig. 1). Large gratings were used in order to ensure that the participant's gaze would be directed toward similar visual stimuli at all times, regardless of eye position during the nystagmus cycle. In addition, gratings provide a robust measure of VA, relying solely on resolution rather than recognition as in the case of optotypes. Twenty square-wave gratings were produced by a high-quality profes-

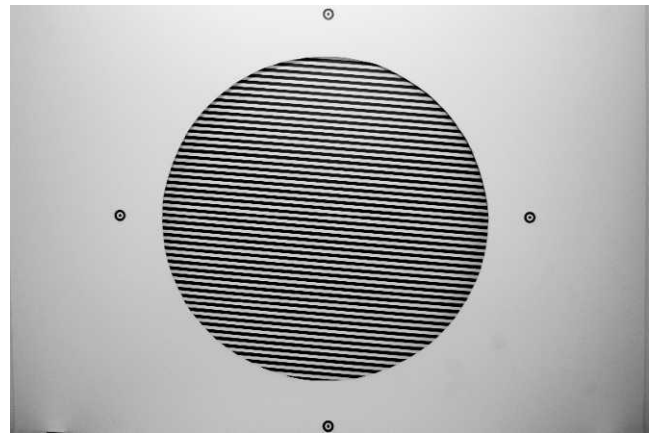


FIGURE 1. Photograph of the aperture frame illuminated by the flash unit, with a grating mounted inside (tilted 5° up to the left), as viewed by subjects. The bull's-eye targets serving as horizontal and vertical axis references can be seen around the grating edge.

sional printer (RA-4 process, Durst Epsilon photographic printer; Durst Image Technology UK Ltd., Surrey, UK) with fundamental spatial frequencies ranging from  $-0.46$  to  $1.48$  logMAR on heat-treated, nonglossy photographic card large enough to fill the 12° aperture.

Four small bull's-eye targets were arranged around the aperture at 90° intervals, providing reference axes (horizontal and vertical) to aid in judgment of tilt. The bull's-eye targets were illuminated by spots of light from a projector, situated behind the subject.

Gratings were illuminated either constantly, by a lamp providing  $1.62$  log cd/m<sup>2</sup>, or tachistoscopically by an unlimited number of flashes each lasting  $0.76 (\pm 0.01)$  ms, from a Metz Mecablitz 76 MZ-5 flash unit (Metz, Zirndorf, Germany) with an output of  $4.64$  cd-s/m<sup>2</sup>. Flash brightness was empirically adjusted in a pilot experiment to provide VA approximately equal to that obtained under constant illumination for one normally sighted individual. Assuming an eye rotating at  $14$  deg/s (the average ocular velocity in IN<sup>22</sup>), a flash of this duration would cause only  $0.01^\circ$  of image smear (allowing a maximum possible VA of  $-0.19$  logMAR). The flash was strobed, with the delay between flashes varying randomly between 2 to 6 Hz in order to prevent flash-timing prediction.

For each presentation, gratings were automatically tilted on a motorized platform either 5° up/down from horizontal or left/right from vertical. Figure 2 shows the tilting mechanism with the aperture removed. Subjects were allowed as much time (or as many flashes) as desired before reporting the perceived tilt direction of each presentation, using a response box. No feedback was given for correct or incorrect responses. The finest grating available that provided a VA equivalent to or worse than the subject's clinical VA (i.e., slightly coarser) was used for the first presentation. Visual acuity was estimated by using a two-alternative forced choice transformed up-down psychophysical staircase procedure of eight reversals with a three-up/one-down criterion. The direction of tilt for any given presentation was decided by combined Gellerman-Fellows sequences.<sup>23</sup> Grating reorientation and flash delivery was automated and computer controlled. The computer identified which grating was to be used next, and the gratings were then physically replaced. Visual acuity was estimated as the mean of the final six staircase reversals.<sup>24</sup>

As mentioned above, this procedure was performed under two different lighting conditions, with gratings oriented about two axes:



FIGURE 2. Computer-controlled platform used for automating grating orientation, shown here with the aperture removed.

- *Constant horizontal*: Gratings oriented  $\pm 5^\circ$  about the horizontal axis, under constant illumination;
- *Tachistoscopic horizontal*: Gratings oriented  $\pm 5^\circ$  about the horizontal axis, illuminated tachistoscopically;
- *Constant vertical*: Gratings oriented  $\pm 5^\circ$  about the vertical axis, under constant illumination; and
- *Tachistoscopic vertical*: Gratings oriented  $\pm 5^\circ$  about the vertical axis, illuminated tachistoscopically.

Test presentation order was randomized.

## RESULTS

The Table shows the data obtained from all 18 subjects, including clinical VA and, for each of the four conditions, grating acuity (logMAR).

The data from the Table are summarized in Figure 3.

Figure 3 shows that, under all illumination conditions and orientations, subjects with idiopathic IN performed significantly worse than controls (all  $P < 0.005$ ). Subjects with idiopathic

IN performed worse for vertically oriented gratings, whereas controls did not show an orientation effect (see below). Most importantly, illumination type did not affect VA for either group. Note that no effect of illumination was expected or observed in the *control* group, since the brightness of the flash was adjusted in a pilot experiment to give approximately the same VA.

## Tachistoscopic Versus Constant Illumination

The effect of tachistoscopic presentation on VA was analyzed by using paired samples *t*-tests. Tachistoscopic presentation caused no significant difference in VA in controls for either orientation (horizontal:  $P = 0.6224$ ; vertical:  $P = 0.0807$ ). Similarly, in nystagmats, there was no significant difference between lighting conditions for either orientation (horizontal:  $P = 0.2311$ ; vertical:  $P = 0.2431$ ).

## Effect of Orientation

Paired samples *t*-tests indicate a significant orientation effect in nystagmats under both constant ( $P = 0.0076$ ) and tachistoscopic ( $P = 0.0188$ ) conditions. For both lighting conditions, near-horizontal grating acuity was better than that for near-vertical gratings. However, the VA for control subjects was not significantly different regardless of orientation under both conditions ( $P = 0.8672$  for constant light and  $P = 0.4426$  for tachistoscopic presentation).

## DISCUSSION

Under all lighting conditions and stimulus orientations, VA was worse for subjects with idiopathic IN than controls. Crucially, the fact that VA did not improve under tachistoscopic illumination suggests that *image motion may not be the limiting factor to VA in IN*. We found no significant difference in VA between constant and tachistoscopic illumination, *even for vertically oriented gratings*. Since all the nystagmats in this study had primarily horizontal nystagmus, if motion blur were a limiting factor to visual perception, one would have expected vertically oriented gratings to be clearer under tachistoscopic

TABLE. VA (logMAR) Recorded for All Subjects

	Subject	Sex	Age, y	Clinical VA	Constant Horizontal	Constant Vertical	Tachistoscopic Horizontal	Tachistoscopic Vertical
Idiopathic IN	GT2	M	59	0.78	0.80	0.86	0.70	0.91
	DB	M	53	0.64	0.65	0.65	0.80	0.65
	JT	M	24	0.42	0.21	0.33	0.33	0.41
	SW	F	69	0.16	0.21	0.37	0.17	0.34
	JC2	F	54	0.54	0.42	0.53	0.34	0.54
	GS	M	28	0.54	0.39	0.51	0.28	0.42
	NB	M	44	0.26	-0.06	0.31	-0.11	0.33
	DP	M	38	0.60	0.16	0.54	-0.02	0.68
	VV	F	21	0.34	0.36	0.46	0.23	0.52
Mean $\pm$ standard error				0.48 $\pm$ 0.07	0.35 $\pm$ 0.09	0.51 $\pm$ 0.06	0.30 $\pm$ 0.10	0.53 $\pm$ 0.06
Controls	LP	F	23	0.10	0.03	0.01	0.17	0.08
	JS2	M	24	-0.16	-0.04	-0.03	0.01	-0.07
	FE	M	47	-0.08	-0.14	-0.11	-0.08	-0.03
	PG	M	20	-0.20	-0.11	-0.14	-0.17	-0.08
	TM	M	48	-0.22	-0.11	-0.03	-0.11	-0.04
	AS	F	23	-0.14	-0.03	-0.06	-0.01	-0.10
	MU	F	21	-0.08	0.03	-0.07	-0.03	0.02
	BF	F	26	-0.10	-0.08	0.01	0.02	0.07
	JT2	M	23	-0.14	-0.09	-0.09	-0.20	0.00
Mean $\pm$ standard error				-0.11 $\pm$ 0.03	-0.06 $\pm$ 0.02	-0.06 $\pm$ 0.02	-0.05 $\pm$ 0.04	-0.02 $\pm$ 0.02

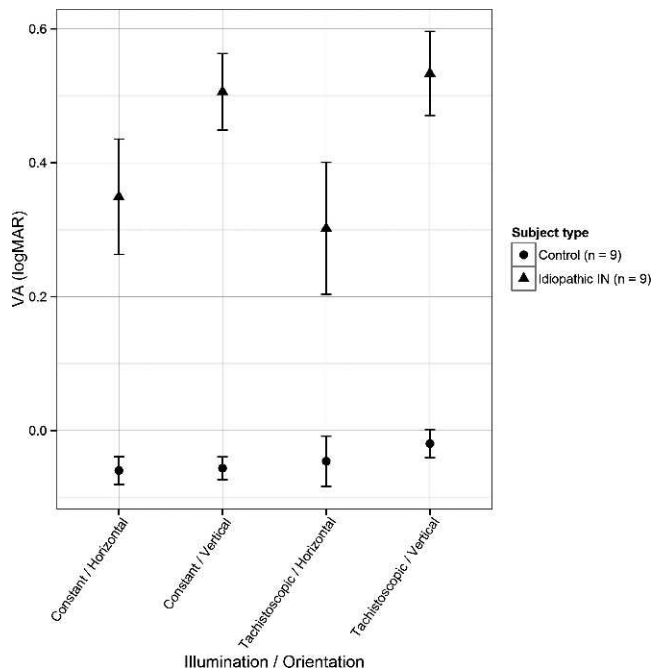


FIGURE 3. Graphical representation of the VAs recorded for all subjects. Error bars indicate standard error.

illumination, resulting in a change in measured VA. Although no effect of illumination was expected in controls (since the flash brightness was set to approximately achieve equality), the absence of a significant improvement in VA in the subjects with idiopathic IN was unexpected.

Under both lighting conditions, subjects with idiopathic IN had significantly poorer VA for vertical gratings than horizontal, whereas controls showed no effect of orientation. This finding is strongly suggestive of meridional amblyopia in IN and has previously been reported under constant illumination.<sup>25</sup> Abadi and King-Smith<sup>21</sup> have found a similar effect under tachistoscopic illumination using a measure of visual sensitivity, although ours is the first study to measure VA under this condition.

Previous studies<sup>2,3,12</sup> have reported a correlation between foveation quality (e.g., duration, accuracy) and VA, and concluded that eye movement characteristics can be used to predict VA. While this has been shown with simulated waveforms in controls and *between* individuals with IN, the correlation does not appear to be evident in response to waveform changes *within* the same subject.<sup>26,27</sup> The results of minimizing image motion in the present study strongly suggest that there is an upper limit on the VA possible in adults with idiopathic IN, and that this limit is independent of eye movement characteristics.

Treatments such as biofeedback have been shown to cause increased foveation duration, but were abandoned owing to the lack of an improvement in VA.<sup>28,29</sup> In light of our unexpected finding indicating that VA cannot be *expected* to improve, it may now be worth revisiting this and other therapies, as there may be other visual benefits that are not captured by VA measurement. For example, we hypothesize that prolonging foveation duration might result in faster visual recognition speed (i.e., reduced visual recognition time), since the retinal locus of highest photoreceptor density would be directed toward the object of interest for a greater proportion of time.

Despite the incessant eye movements, adults with IN usually do not experience oscillopsia,<sup>18</sup> but regardless of this stable percept, retinal anatomy dictates that vision *cannot* be

optimal when the fovea is not directed at the locus of attention. It is hardly surprising therefore that VA, a static measure of visual function in which viewing time is unlimited, cannot adequately represent the visual experience of those with nystagmus.

Algorithmic measures of waveform characteristics (such as Nystagmus Optimal Fixation Function and NAFX) are designed to quantify visual performance, but these are currently predicated on the presumed relationship between VA and foveation characteristics. Alternative assessments might measure other aspects of visual performance, such as processing speed (e.g., time-restricted optotype recognition tasks<sup>30</sup> or visual response speed measurements<sup>31</sup>) or target acquisition timing.<sup>32</sup> Ideally, these measures would correlate with foveation characteristics and subjective visual experience better than VA.

Image motion blur can have a deleterious effect on vision in normal subjects, which has understandably led to an assumption that the blur induced by the oscillations in IN is, at least partly, responsible for their reduced VA. However, previous studies<sup>27,33,34</sup> have found little if any significant change in subjects' VA as a result of modifications to their eye movements, whether produced by varying gaze angle, stress, or task demand. Moreover, although treatments for nystagmus are often designed to reduce the velocity of the eye movements, they rarely elicit improvements in VA, whether using optotypes for recognition acuity<sup>15,35,36</sup> or its prerequisite, resolution acuity, as measured by gratings in the present study.

The results of the present study indicate that removing the image motion blur altogether in subjects with IN also does not change VA, suggesting that their VA may already be fundamentally limited, owing to an underlying pathology and/or stimulus deprivation amblyopia as a result of motion blur during the critical period for visual development. One view on the pathogenesis of IN is that it is a developmental adaptation to enhance contrast in the presence of a pre-existing visual acuity deficit.<sup>37-39</sup> If this is the case, then the parameters of the adult waveform (foveation duration, average eye velocity, etc.) may well reflect the maximum VA that was available in infancy. This would explain the strong correlation between, for example, foveation duration and VA *across* subjects.<sup>10</sup> In other words, poor-quality nystagmus waveforms may not lead to poor VA; rather, the properties of nystagmus waveforms in adults may reflect the underlying VA, as suggested by a recent study on the development of IN.<sup>40</sup> For these reasons, interventional studies are likely to require better outcome measures than VA alone if they are to demonstrate an objective change in visual performance.

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