Measurement of visual function in infantile nystagmus: A systematic review

Bader A Almagren[1,2], Nystagmus U.K. Eye Research Group (NUKE), Matt J Dunn[2]

Nystagmus U.K. Eye Research Group (NUKE): Gemma Arblaster[3,4], Perry Carter[5], Jonathan T Erichsen[2], Helen Griffiths[6], Christopher M Harris[7], Harshal Kubavat[8], Helen Kuht[9], Helena Lee[10], Rebecca McLean[9], Lee McIlreavy[2], Frank A Proudlock[9], Sue Ricketts[8], Jay E Self[10], Fatima Shawkat[5], Maria Theodorou[11], Mervyn Thomas[9], Nikita Thomas[12], Katherine Ward[2], J Margaret Woodhouse[2]

[1] Optometry Department, College of Applied Medical Science, King Saud University, Riyadh, Saudi Arabia
[2] School of Optometry and Vision Sciences, Cardiff University, Cardiff, UK
[3] School of Allied Health Professions, Nursing and Midwifery, University of Sheffield, UK
[4] Orthoptist Department, Sheffield Teaching Hospitals NHS Foundation Trust, UK
[5] The Eye Unit, University Hospital Southampton NHS Foundation Trust, Southampton, UK
[6] Sheffield Children's Hospital, Sheffield, UK
[7] Royal Eye Infirmary, Derriford Hospital, Plymouth, UK
[8] Nystagmus Network, UK
[9] Faculty of Medicine and Biological Sciences, University of Leicester, Leicester, UK
[10] Clinical and Experimental Sciences, Faculty of Medicine, University of Southampton, Southampton, UK
[11] Paediatric Ophthalmology and Strabismus, Moorfields Eye Hospital, London, UK
[12] Vision and Hearing Sciences Research Centre, Anglia Ruskin University, Cambridge, UK

Correspondence to:

Dr Matt J Dunn
School of Optometry and Vision Sciences
Cardiff University
Maindy Road
Cardiff CF24 4HQ, Wales, UK

Tel: +44 (0)29 20870576

Email: DunnMJ1@cardiff.ac.uk

Synopsis/Précis: The suitability of visual acuity to measure changes in visual function in infantile nystagmus (IN) has long been debated. No appropriate alternative yet exists. Several factors have been shown to affect visual performance in IN.

Abstract

Background/Aims: Recent work has called into question the ability of visual acuity (VA) to accurately represent changes in visual function in infantile nystagmus (IN). This systematic review investigated factors affecting visual performance in IN, to guide development of suitable alternatives to VA.

Methods: Included studies used an experimental manipulation to assess changes in visual function in people with IN. Interventional studies, case series and case studies were excluded. Six databases were searched in August 2023. Selection, detection, attrition, and measurement bias were assessed. Due to heterogeneous methodologies, narrative synthesis was undertaken.

Results: Eighteen relevant papers were identified, eleven of which obeyed the review criteria. Articles were grouped according to the factor manipulated to evoke within-participant changes in performance (motion blur, psychological state, gaze angle or visual crowding). Optotype, image, grating and moving stimuli have been employed under varying lighting conditions and exposure durations.

Conclusion: Several factors affecting visual performance should be considered when assessing visual function in IN. While maximum VA is a useful metric, its measurement deliberately minimises nystagmus-specific factors such as changes in visual performance with gaze angle and the 'slow to see' phenomenon. Maximum VA can be measured using the null zone, providing unlimited viewing time, reducing stress/mental load and minimising visual crowding. Gaze-dependent functional vision space is a promising measure which quantifies the impact of the null zone but does not consider temporal vision. Although no complete measurement technique has yet been proven, this review provides insights to guide future work towards development of appropriate methods.

What is already known in this topic: Several factors that affect visual function in infantile nystagmus (IN) have been investigated in experiments utilising various measurement techniques. Some of these approaches have the potential to be adopted or standardised in nystagmus clinics or future research studies.

What this study adds: A clinician's guide of factors to consider when measuring visual function in IN. This review highlights that visual acuity measurement in isolation is not appropriate to measure visual function in IN and provides insights for future research aiming to establish appropriate methods. The inability to properly measure visual function limits the interpretation of clinical trials – real improvements in visual function may be missed using current metrics.

How this study might affect research, practice, or policy: Clinicians and researchers should consider controlling the various factors identified in this review when measuring maximum VA. The results of this review should help guide research efforts to design and adopt appropriate measurement technique(s).

Introduction

Nystagmus is characterised by repetitive involuntary eye movements (see Figure 1). Infantile nystagmus (IN) is an early-onset nystagmus, typically developing around 1.9 months of age[1] and persisting for life. IN is relatively uncommon; a survey in England found a prevalence of 0.14%.[2] IN often occurs in conjunction with visual system pathology. If no underlying cause can be identified, the condition is labelled idiopathic infantile nystagmus (IIN). Vision is reduced in people with IIN: a study examining sight test records from 224 patients with IN found an average visual acuity (VA) of 0.55, 0.67 and 0.35 logMAR for groups with associated ocular anomalies, albinism and IIN, respectively.[3] Nonetheless, some patients achieved VA < 0.00 logMAR. A more recent study measured VA using gratings in children with IIN, finding an average VA of 0.25 logMAR.[4]

The fact that visual function is reduced in IIN has historically led to the assumption that eye movements blur the retinal image, degrading visual performance. Studies in typically-sighted observers demonstrate that motion degrades VA – Barnes and Smith[5] found a significant decline for stimuli moving at ≥4°/s, although other studies[6-8] suggest a threshold closer to 2.5°/s. The average velocity throughout an IN waveform is ≈14°/s.[9] One might therefore reasonably conclude that nystagmus actively degrades visual performance. However, IN waveforms typically include *foveation periods* during which the eye movements slow, and these have the potential to provide 'snapshots' of relatively clear vision. Note that the term 'visual function' should not be confused with *functional vision*, which describes the ability to perform visual tasks such as reading.

Foveation periods typically develop at around three years of age.[4] Constant exposure to undampened oscillations prior to this age raises the possibility that bilateral motion blur-induced amblyopia fundamentally limits VA later in life. Previous research has investigated the impact of motion blur on VA, using tachistoscopic stimulus presentation to eliminate the potential impact of motion blur. Dunn et al.[10] found no change in VA with tachistoscopic presentation and argued that motion blur does not limit VA in adults with IN, suggesting that the effects of motion blur are already 'locked in' by adulthood in the form of amblyopia, although undetected visual system disorders cannot be excluded. Huurneman et al.[11] trialled a computerised vision training therapy in children with IN, yielding improvements in both VA and stereopsis. The same protocol has been shown to yield comparable results in patients with amblyopia,[12] suggesting a similar mechanism of vision loss may be responsible in IN.

Others have speculated that oscillopsia (perception of an oscillating visual scene) disrupts perception of high spatial frequencies, preventing people with IN achieving optimal/normal VA. Oscillopsia is typically absent in adults with IN[9] yet may be provoked in certain situations such as under stress or monocular viewing[3].

Many studies have investigated the concept that individuals with IN require longer exposure time to recognise visual stimuli, although the exact nature of this 'slow to see' phenomenon is not fully understood. Huurneman et al.[13] asked children with IN to search for a target among distractors and found children with IN to be slower than controls. However, the level of performance was comparable to a vision loss group without nystagmus, suggesting that the issue may not be nystagmus *per se*, but a general result of having reduced VA. A more recent study measured the time for children to find a familiar image among unfamiliar images, finding that children with IN typically took 1.41 s longer than controls.[14]

Other factors such as gaze angle, stress, and mental load have all been shown to affect visual function in IN. This systematic review summarises studies that measure within-individual changes in visual performance in IN and discusses how the methods employed could guide efforts to develop appropriate methods of assessing visual function.

Methods

Following a scoping search to determine appropriate keywords (using PubMed and Google Scholar), a search was conducted across six databases: PubMed, EMBASE, Scopus, CINAHL, Web of Science and The Cochrane Library on 30th August 2023. Free text search terms were combined as follows: (infan* OR child* OR congenital OR idiopathic) AND (nystagmus OR oscillation) AND (visual OR vision OR acuity OR perception). Studies were included if a sensory measure was used in people with IN to assess within-participant changes in visual function resulting from either manipulation of nystagmus eye movements (e.g., by comparing performance at different gaze angles), or manipulation of a stimulus to indirectly investigate the impact of nystagmus eye movements (e.g., gaze-contingent stimuli). Grey articles and reference lists were inspected to identify additional articles. The search was limited to articles in English and studies involving participants without active ocular disease (other than IN). Interventional studies (e.g., medical/surgical trials) were excluded owing to an unavoidable measurement order effect. Reports of case series and case studies were not included as bias is generally considered to be higher. Figure 2 summarises the search process. Many articles screened out at the abstract stage did not use a sensory measure of visual function, using instead motor-based measures such as NAFX[15], which do not measure visual function, but predict it based on nystagmus characteristics.

Data collection

A form was used to standardise the selection of appropriate articles (see Appendix A). Studies were excluded if they did not clearly identify the sample (diagnosis, sex, disease, age, etc.) Full-text inspection of 24 papers found 18 (see Appendix B[31-35]) that obeyed the criteria for critical appraisal. Seven of these failed the assessment (see Appendix C for justifications). The remaining 11 articles were included in this systematic review, all of which were quasi-experimental studies. The review was not pre-registered.

Bias assessment

Four of the most common bias risks in quasi-experimental study designs were assessed: selection, detection, attrition, and measurement bias. Possible confounding factors were discussed.

Data synthesis

Owing to the diversity of methodologies and sample heterogeneity, meta-analysis was not possible. Therefore, a narrative synthesis was undertaken. Included studies were divided into groups based on the manipulated factor (e.g., psychological state, gaze angle). Each sample group was discussed individually for the same reason.

Results

The studies included in this review (summarised in Table 1) employed a broad range of techniques to elicit within-participant changes in visual performance. Simmers et al.[21] and Dunn et al.[10] each investigated the impact of eye oscillations on VA by reducing potential sources of visual degradation (the effect of the eye being off-axis during non-foveating periods and motion blur, respectively). Jones et al.[22] and Fadardi et al.[23] assessed the impact of stress and mental load on VA, respectively. Costa et al.[24], Dunn et al.[25] and Roberts et al.[26] assessed the impact of gaze angle on VA, while two studies by Dai et al.[27-28] assessed its impact on motion perception. Pascal and Abadi[29] and Tailor et al.[30] each assessed the impact of visual crowding in IN.

Eye movement

Motion blur and fixation inaccuracy resulting from the eye movements are intuitive explanations for poor vision in IN. Simmers et al.[21] employed the Regan Repeat Letter (RRL) chart to minimise the effect of fixation inaccuracy on VA. The RRL chart repeats the target optotype across a central array, surrounded by non-target optotypes (see Figure 3). VA measured using the RRL chart was compared to that obtained with the logMAR Crowded Test (Keeler, Windsor, UK) which shows a single optotype with bar flankers. Dunn et al.[10] minimised retinal image motion by illuminating grating stimuli with flashed light, comparing this to a constant illumination condition. Both studies had a comparable sample size, mean age and sex balance, and both studies had normally-sighted control groups. Simmers et al.[21] concluded that the RRL chart provides a more accurate estimate of maximum VA. VA in the IN group was higher by an average of more than two lines using RRL (0.88 ±0.21 logMAR), as compared with Keeler (0.64 ±0.23) (p = 0.0004), whereas there was no significant difference between the charts in the control group (RRL [1.21 ±0.07], Keeler [1.19 ±0.07], p = 0.17). On the other hand, Dunn et al.[10] found that eliminating retinal image motion had no significant effect on VA in either group: when viewing vertically-oriented gratings under constant illumination, VAs were 0.51 ±0.06 logMAR and -0.06 ±0.02 for IN and controls respectively, and 0.53 ±0.06 and -0.02 ±0.02 under tachistoscopic conditions. Taken together,

these studies indicate that fixation inaccuracy, but not motion blur, degrades visual performance in adults with IN, and that the RRL chart may provide a suitable means to minimise the effect of fixation inaccuracy when measuring maximum VA.

Psychological state

Using electric shocks as a stressor, Jones et al.[22] concluded that stress does not significantly impact VA in people with IN. Participants were tested under three conditions: one in which a shock was given for every incorrect answer, one in which shocks were delivered at random, and a condition without shocks. Stress was confirmed by galvanic skin resistance. Despite having no significant effect on VA, stress affected response times and all measured waveform parameters except frequency (reaction time $p = 0.009$, amplitude $p = 0.01$, intensity $p = 0.007$, foveation duration $p = 0.022$, frequency $p = 0.14$).

To induce high mental load, Fadardi et al.[23] asked participants to solve mathematical problems while reporting the orientation of a time-restricted (1.8 s) Tumbling E. Another condition required participants to identify orientation only, with no time restriction or distractors. Tumbling Es were modified both in contrast and size according to a prearranged sequence. High mental load significantly degraded visual performance but had no significant main effect on waveform characteristics. However, there was a significant interaction effect between mental load and gaze position on both foveation duration and visual performance, indicating that mental load impacts on waveform characteristics and visual performance when viewing away from the null zone.

Taken together, these studies indicate that (1) stress does not affect VA whereas mental load has been shown to affect visual performance in a combined contrast/VA task; and (2) stress significantly impacts waveform characteristics, and mental load – while having no significant impact on the waveform in general – has greater influence on the waveform when patients use a gaze angle away from the null zone.

Gaze angle

The null zone is the range of gaze angles at which nystagmus intensity is lowest. Around 30% of patients with IN adopt an abnormal head posture to use this angle,[3] and patients report improved visual quality when using the null zone. Costa et al.[24] measured VA in 11 young children with IN (mean age 4.3 years) at the null zone versus straight ahead. They found significant improvements in VA ($p = 0.006$) with the null zone. In a similar study of an adult population (mean age 33 years), Dunn et al.[25] assessed VA at three gaze angles including the primary position, null zone and an angle away from the null zone. Waveform characteristics (amplitude, foveation precision and foveation duration, but not frequency) were significantly correlated with VA across individuals with nystagmus (amplitude $p = 0.003$, foveation precision $p = 0.009$, foveation duration $p < 0.0001$), but *within* any given individual, there was no significant correlation between gaze angle and any of the waveform parameters. There was however a

small but significant VA improvement at the null zone (0.08 logMAR). Therefore, it is appropriate to encourage patients to adopt their null zone to measure maximum VA.

Using a different approach, Roberts et al.[26] proposed a new quantifying function known as gaze-dependent functional vision space (GDFVS). To calculate GDFVS, VA is measured at horizontal gaze angles spanning the central 60° of visual space in 10° steps. The area under the curve (logMAR vs gaze angle) is subtracted from the total graph area, using a ceiling of 1.30 logMAR. Thus, GDFVS reflects the variability of VA across the 60° range. Roberts et al.[26] repeated VA measurement twice at each gaze angle and found no significant difference and a high interclass correlation coefficient (≥ 0.97) in patients with IN. The authors concluded that relying solely on maximum VA does not provide a complete measure of visual function in IN, and recommended GDFVS to address this.

In two studies by Dai et al.[27-28], the impact of gaze angle on velocity discrimination and coherent motion perception was assessed for horizontal and vertical motion at two gaze angles; at the null zone and 15° away from it (for nystagmats), or at primary gaze and 20° away in the case of control participants. In the velocity discrimination study[27], stimuli were high contrast drifting gratings presented within a Gaussian window. Using a two-alternative forced choice staircase procedure, participants indicated the faster of two successively presented gratings; one at 5°/s and the other ranging from 5-10°/s. The coherent motion study used 100 limited-lifetime dots travelling at 10°/s, shown for 650 ms within a 10° aperture.[28] Participants with IN performed worse than controls in both tasks. In addition, nystagmats with an identified null zone had lower thresholds for horizontal motion; this difference was significant for velocity discrimination but not for coherent motion.[27-28] Significantly higher horizontal thresholds were found in the velocity discrimination task ($p < 0.001$), but there was no significant difference between vertical and horizontal thresholds for coherent motion perception ($p = 0.2921$). Dai et al.[27-28] concluded that both velocity discrimination and coherent motion perception are impaired in individuals with IN, and that employing the null zone improves velocity discrimination, but not perception of coherent motion.

Crowding

The presence of neighbouring letters or other distractors around a stimulus makes recognition more difficult due to the crowding effect.[31] Pascal and Abadi[29] recruited three groups of six participants (controls, IIN and albinos) to test the impact of crowding and contrast. The study involved three levels of contrast (94%, 34%, 12%) and crowding (isolated, near or distant flankers). Using Landolt Cs to measure VA, all groups were influenced by crowding; however, only the IIN group showed a significant difference.

Also using Landolt Cs, Tailor et al.[30] recruited eight people with IIN, 10 strabismic amblyopes and 10 controls to measure the impact of visual crowding. Targets were flanked either horizontally or vertically by oblique Cs. Participants reported target orientation without time restrictions. Although insignificant,

controls and amblyopic participants had lower thresholds for vertical than horizontal crowding. In contrast, all participants with IN had significantly higher (p = 0.001) thresholds with horizontal crowding. The authors attributed this elevation in threshold to nystagmus eye movements, which are predominantly horizontal. Further analysis of eye position, velocity, and foveation periods showed no correlation.

Table 1: Summary of the reviewed articles

Study of	Study	Key findings	Sample diagnosis: sex, mean age (if stated)	Stimulus type: Distance / Viewing condition / Time restriction
Eye movement	Simmers et al. 1999	VA is better with the RRL chart than Keeler, indicating that fixation inaccuracy limits VA in adults with IN.	5 IN: 4♂/1♀, mean = 35 yrs 10 controls: 4♂/6♀, mean = 26.7 yrs	Keeler vs RRL chart 2 m / Monocular / Unrestricted
	Dunn et al. 2014	Brief illumination (0.76 ms) of a stimulus does not improve VA as compared to constant illumination, indicating that motion blur does not limit VA in adults with IN.	9 IIN: 6♂/3♀, mean = 43 yrs 9 controls: 5♂/4♀, mean = 28 yrs	Square-wave grating 2 m / Monocular / Unrestricted vs 0.76 ms
Psychological state	Jones et al. 2013	Introducing a stressor shortens foveation periods and lengthens response time but does not affect VA, indicating that stress does not limit VA in adults with IN.	19 IIN, 4 albino: mean = 44 yrs 20 controls: mean = 34 yrs	Landolt C 7 m / Binocular / Unrestricted
	Fadardi et al. 2017	High mental load significantly degrades performance in a mixed contrast sensitivity / VA task, indicating that mental load limits visual function in adults with IN.	11 IIN: 8♂/3♀, mean = 31 yrs	Tumbling E 0.16 m / Monocular / Unrestricted vs hurried by examiner
Gaze angle	Costa et al. 2013	Viewing with the null zone in children significantly improves VA compared to primary gaze viewing, indicating that gaze angle limits VA in children with IN.	11 IN: mean = 4.3 yrs	Lea grating 0.5 m / Binocular / Unrestricted
	Dunn et al. 2017	Employing the null zone significantly improves VA, indicating that gaze angle limits VA in adults with IN.	8 IIN: 5♂/3♀, mean = 33 yrs	Landolt C 7 m / Binocular / Unrestricted
	Roberts et al. 2018	GDFVS measures the impact of the null zone on VA and is a reliable and valid method to quantify visual function.	20 IN: mean = 15.6 yrs 14 controls: mean = 42.1 yrs	Single flanked optotype 3 m / Binocular / Unrestricted
	Dai et al. 2021	Employing the null zone improves velocity discrimination in adults with IN.	18 IIN, 2 albino, 1 congenital cataract: 7♂/14♀, mean = 26 yrs 16 controls: mean = 26 yrs	Sinusoidal grating 0.75 m / Binocular / Restricted
	Dai et al. 2022	Gaze angle has no impact on coherent motion perception in adults with IN.	20 IIN, 1 albino: 7♂/15♀, mean = 23.95 yrs 13 controls: mean = 27 yrs	Random dot kinematogram 0.75 m / Binocular / Restricted
Crowding	Pascal and Abadi 1995	Crowding significantly degrades VA in IN, indicating that crowding limits VA in adults with IN.	6 IIN, 6 albino: 4♂/8♀, mean = 26 yrs 6 controls: 3♂/3♀, mean = 28 yrs	Landolt C Varied / Monocular / Unrestricted
	Tailor et al. 2021	Horizontal flankers have a significant impact on VA in people with IN, indicating that horizontal crowding can limit VA in IN.	8 IIN: mean= 30.3 yrs 10 controls: mean = 32.1 yrs	Landolt C Varied / Binocular (for IN) / Unrestricted

Risk of bias

Most studies included in this systematic review were deemed to have an overall medium or low risk of bias, with one having high risk (see Table 2). An overall high risk was identified when more than one high risk, or more than two medium risks were present. Selection bias was potentially present due to unclear recruitment procedures in five studies[21, 26-28, 30]. Detection bias is introduced when the method of measuring study outcomes is not identical in each group and is minimised by either single or double-blinding. In nystagmus studies, it is difficult to blind researchers to the presence of nystagmus due to obvious eye movements and comorbid conditions (such as albinism). Tailor et al.[30] used different viewing distances both between and within groups; changes in convergence angle can impact nystagmus intensity[32]. Measurement bias was present or potentially present in almost every study. Dunn et al.[10] provided a new prescription to participants who had a ±0.50 DS difference; this should ideally include a period of adaptation. Three studies[22-24] failed to counterbalance the order of conditions/tasks, yet based their conclusions on comparing the differences between these. Three other studies[21, 25, 30] did not report whether test order was counterbalanced. Although Pascal and Abadi[29] stated that half of participants performed one of the conditions first, it was unclear whether this included counterbalancing within groups.

Table 2: Risk of bias assessment based on authors' judgment.

		Selection	Detection	Attrition	Measurement	Overall
	Pascal and Abadi 1995[29]	+	+	+	?	+
	Simmers et al. 1999[21]	?	+	+	?	?
	Jones et al. 2013[22]	+	+	+	-	?
	Costa et al. 2014[24]	+	+	+	-	?
Study	Dunn et al. 2014[10]	+	+	+	?	+
	Dunn et al. 2017[25]	+	+	+	?	+
	Fadardi et al. 2017[23]	+	+	+	-	?
	Roberts et al. 2018[26]	?	+	+	+	+
	Tailor et al. 2021[30]	?	-	+	?	-
	Dai et al. 2021[27]	?	+	+	+	+
	Dai et al. 2022[28]	?	+	+	+	+

— = high risk; **+** = low risk; **?** = unclear

Discussion

The current evidence base is insufficient to support clinical use of specific method(s) for measuring visual function in IN. Developing an appropriate test of visual function first requires an understanding of the various factors affecting vision. It is important to distinguish between the measurement of *maximum VA* (which necessarily minimises these factors to determine visual resolution) versus measurement of the factors themselves, which constitute the *nystagmus-specific visual impairment*. While the studies focused on by this review provide insights into which factors matter and how to minimise them when measuring maximum VA, little progress has been made toward quantifying the factors themselves, nor is it understood the extent to which underlying pathology interacts with these factors.

One such factor is fixation inaccuracy resulting from the eye movements.[21] The RRL chart, being less dependent on fixation stability, is better suited to measuring maximum VA than a traditional letter chart. A second factor – gaze angle – has been shown to significantly affect both velocity discrimination[27] and VA,[24, 25] and the null zone should be adopted when measuring maximum VA (which may preclude the use of phoropters in clinical practice); any test to quantify nystagmus-specific visual impairment should consider this. GDFVS therefore provides a more complete representation of visual function since it considers the impact of gaze angle[26]. Another potential factor – which was not the subject of any of the reviewed articles – is periodic alternating nystagmus, an additional confounder in some individuals with IN for whom nystagmus intensity varies as a function of time[33]. Psychological factors such as mental load and stress are also known to impact upon nystagmus characteristics, but only mental load has been shown to measurably affect visual performance[23]. This indicates that mental load should be reduced when assessing maximum VA. 'Mental load' should not be confused with 'stress' which does not significantly affect VA, despite exacerbating the nystagmus waveform. Although stress does not degrade VA, it increases response times,[22] which are known to be slower in IN than in normally-sighted individuals[14, 23, 34]. Therefore, clinicians should be mindful to put patients at ease and avoid rushing when measuring maximum VA.

Since visual performance is affected by a range of factors, we recommend that, until suitable methods are available to quantify those factors, interventional studies should consider these as potential confounders to be controlled. Objective tests such as visual evoked potentials, which are particularly useful in infants and individuals who are unable to perform standard VA tests, may also be worth exploring. While no suitable measure currently exists to *directly* measure nystagmus-specific changes in visual function, clinicians could consider questionnaire-based approaches[35], which despite being indirect measures of past experience, provide a means to describe the impact of visual impairment on daily functioning.

To date, there is not enough evidence to recommend a single reliable method or group of methods to assess visual function in people with IN. The RRL chart shows promise in terms of measuring maximum VA, so long as it is presented without time restrictions, stress or mental load, and viewed using the null

zone. Single letter stimuli avoid the crowding effect which may degrade VA to a greater degree in IN, particularly for horizontal crowding[29, 30]. Whilst maximum VA may be a useful metric in certain circumstances, the measurement of maximum VA deliberately ignores the impact of both the null zone and temporal visual function, both of which are specific to nystagmus. GDFVS is a promising technique that considers the impact of the null zone but provides no insight into temporal visual function. A complete measure of nystagmus-specific visual impairment should describe both the impact of the null zone *and* temporal visual impairment. Further work is necessary to determine whether this can be achieved by a single test, or if a multifactorial approach is more appropriate.

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Figures
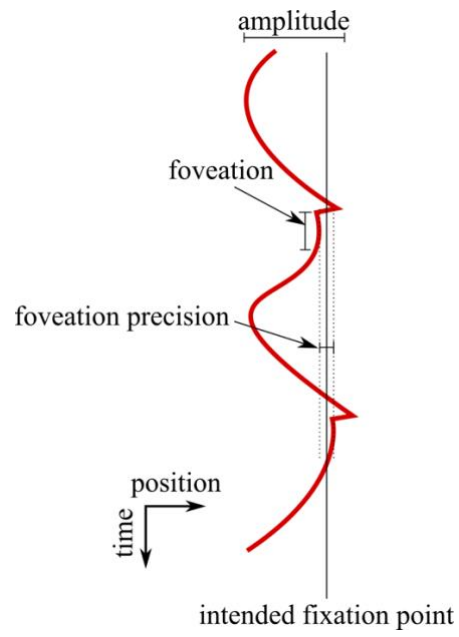
Figure 1: Schematic of a nystagmus eye position waveform (pendular with foveating saccades)
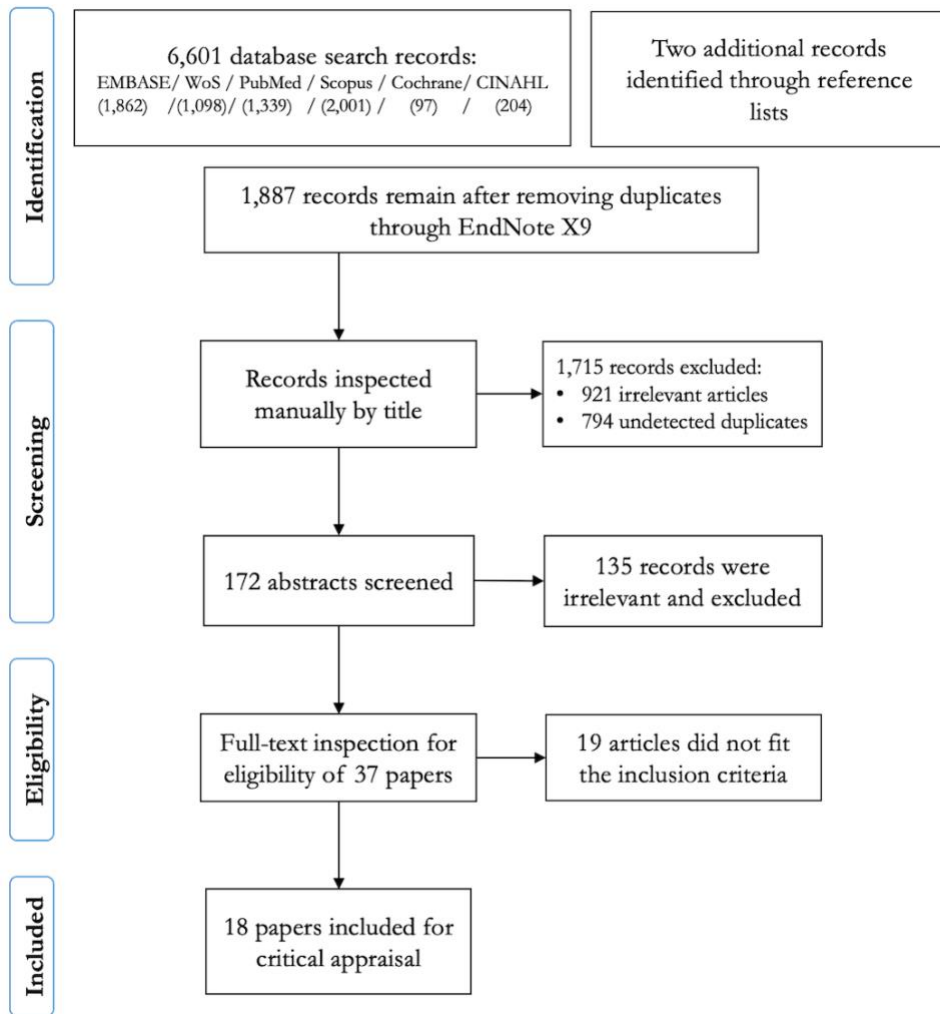
Figure 2: PRISMA 2009 flow diagram representing the search process

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H K O H H R H V Z S K O D
Z V V H O C N K D D N C O
N R R R C C K O R R V S Z
O K D N N N N N N N H O N
V O Z N N N N N N N C H H
R V K N N N N N N N O N N
S K S N N N N N N N R D S
H Z H N N N N N N N S R R
R R Z N N N N N N N R S K
R N V N N N N N N N K D Z
R N R O R O S O Z H D D C
N N K S R S Z Z D D R C O
O V N K R S O K D O H C S
```

Figure 3: Array of optotypes as laid out in a RRL chart, in which 'N' is the target letter

Appendices

Paper details			
Author: Simmers, A. et al.	**Year of publication**: 1999	**Study ID**: Pre# 15	**Review date**: 12/08/2020

Title: The effect of abnormal fixational eye movements upon visual acuity in congenital nystagmus			

PICO	Included	Excluded
Population	- IN only - Mixed groups with separate results	- Other types of nystagmus - Mixed groups and mixed results
Intervention	Visual measurement device	- Surgical - Pharmacological
Comparators	*RRL versus logMAR crowded acuity chart*	
Outcomes	*RRL is significantly better estimate of VA in IN owing to limited effect by image motion*	
Study design	Any design but case series or case study	- Case series - Case study
Obey PICO?	YES	NO

*Appendix B: Using the appraisal tool by JBI for quasi-experiment study design. All studies were suitable for the same tool. * = within subject control.*

The question / The study	Abadi and King-Smith 1979[16]	Chung and Bedell 1995[17]	Pascal and Abadi 1995[29]	Chung and Bedell 1997[18]	Simmers et al. 1999[21]	Hertle et al. 2002[19]	Yang et al. 2005[34]	Jones et al. 2013[22]	Costa et al. 2013[24]
Is it clear what is the 'cause' and what is the 'effect'?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the participants included in any comparisons similar?	Unclear	Unclear	Unclear	Unclear	No	Unclear	Yes	Unclear	Yes
Are the participants included in any comparisons receiving similar treatment, other than the exposure	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Was there a control group?	Yes*	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes*
Were there multiple measurements of the outcome both pre- and post-intervention?	No	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes
Was follow up complete and were follow-up differences within groups adequately described and analysed?	NA	Unclear	NA	NA	NA	NA	NA	Yes	NA
Were the outcomes of participants included in any comparisons measured the same way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were outcomes measured in a reliable way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were appropriate statistical analyses used?	Unclear	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Unclear

The question \ The study	Dunn et al. 2014[10]	Dunn et al. 2017[25]	Fadardi et al. 2017[23]	Roberts et al. 2018[26]	Weaterton et al. 2021[14]	Bedell and Song 2021[20]	Tailor et al. 2021[30]	Dai et al. 2021[27]	Dai et al. 2022[28]
Is it clear what is the 'cause' and what is the 'effect'?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the participants included in any comparisons similar?	Yes	Yes	Yes	No	Yes	Unclear	Yes	Unclear	Unclear
Are the participants included in any comparisons receiving similar treatment, other than the exposure	Yes	Yes	Yes	No	Yes	Yes	Unclear	Yes	Yes
Was there a control group?	Yes	Yes*	Yes*	Yes	Yes	Yes	Yes	Yes	Yes
Were there multiple measurements of the outcome both pre- and post-intervention?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was follow up complete and were follow-up differences within groups adequately described and analysed?	NA	NA	No	Yes	No	NA	Yes	NA	NA
Were the outcomes of participants included in any comparisons measured the same way?	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes
Were outcomes measured in a reliable way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were appropriate statistical analyses used?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Appendix C: Reasons for excluding studies which were eligible for critical appraisal.

Study	Reasons for exclusion
Abadi and King - Smith 1979[16]	• Unclear inclusion /exclusion criteria and selection methods • Small sample size • Various missing details (clinical VA, recruitment, other details of the experiment, age, and sex)
Chung and Bedell 1995[17]	• Unclear inclusion /exclusion criteria and selection methods • Small sample size • Various missing details (recruitment method, age, sex, and other details of the experiment) • Different testing method between groups.
Chung and Bedell 1997[18]	• Unclear inclusion /exclusion criteria and selection methods • Small sample size • No detail about possible confounding factors, different testing method between groups.
Hertle et al. 2002[19]	• No detail regarding possible confounding factors • No statistical analysis
Yang et al. 2005[34]	• Unclear inclusion/exclusion criteria and selection methods • Incomplete methods reporting • Statistical methods not described, and p-value not provided for impact of gaze angle on VA
Weaterton et al. 2021[14]	• Unclear whether participants were confirmed as having IN or other forms of nystagmus
Bedell and Song 2021[20]	• Small sample size • Various missing details (controls' VA, recruitment method, age, and sex)