

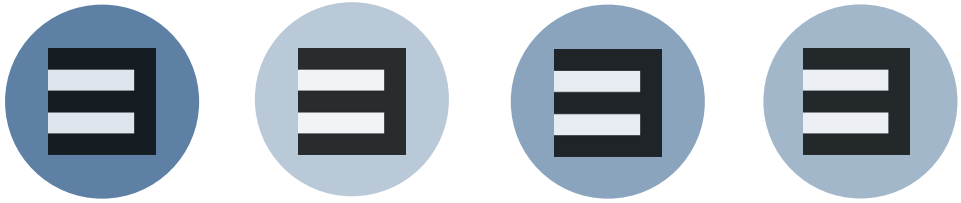
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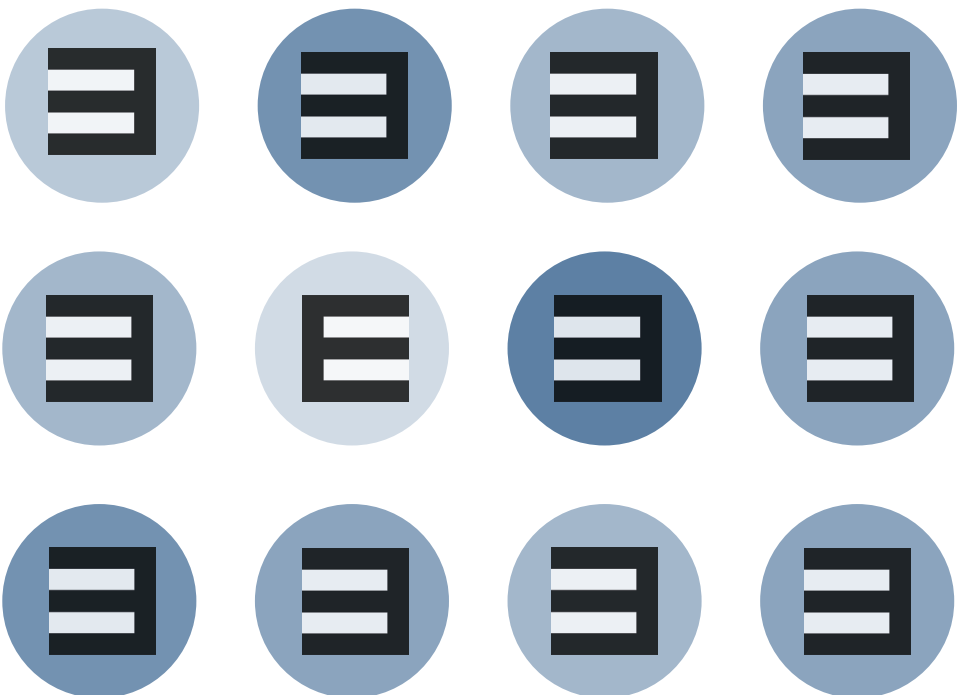
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*Crowding in children with visual  
impairment:  
Improving vision through perceptual  
learning*



Crowding in children with visual impairment



# Crowding in children with visual impairment: Improving vision through perceptual learning

*'All men by nature desire to know. An indication of this is the delight we take in our senses; for even apart from their usefulness they are loved for themselves; and above all others the sense of sight. For not only with a view on action, but even when we are not going to do anything, we prefer seeing (one might say) to anything else. The reason is that this, most of all senses, makes us know and brings to light many differences between things.'*

Aristotle in *Metaphysics* (translated by William David Ross).

Oxford: Clarendon Press, 1924.

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Improving vision through perceptual learning

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chapter



General  
introduction



## Introduction

Imagine standing in an airport. Above your head, there is large board displaying the information you need to arrive at the right terminal. How do you find your way through this complex visual environment? Naturally, you need a goal. What time is my flight? In order to find the desired flight information specific skills are addressed. First, eye movements have to be made, because the board contains too much information to find the target in a single glance. Information from the visual field can be used to move your eyes towards the area of interest, thereby bringing it to the most sensitive part of the retina. Next, visual selective attention is needed to filter out relevant from irrelevant information. With a normal working visual apparatus this whole endeavor does not pose any problems. Now, imagine having great difficulty with distinguishing the target information, because you have difficulty with holding steady fixation (due to involuntary ocular oscillations), or because you have low visual acuity, or because you experience difficulty suppressing surrounding information. The impaired recognition of a suprathreshold target due to the presence of distracting elements in the neighbourhood of that target, is called crowding (Tyler & Likova, 2007).

Crowding is a phenomenon that occurs during normal visual development. Clinically, it can be measured by using vision charts and calculating a crowding ratio (single acuity/line acuity). Crowding can also be measured by means of psychophysiological experiments by measuring the magnitude (the amount of loss of acuity when interaction is at its maximum), and/or extent (maximum distance from the test letter at which the contour degrades recognition: Flom, 1991). Classically, crowding has been said to include: (i) contour interaction, i.e. the effect of nearby contours on the resolution of a single visual target (Flom, Heath, & Takahashi, 1963; Flom, Weymouth, & Kahneman, 1963), (ii) attentional factors, and (iii) fixational eye movements (Flom, 1991). Contour interaction areas do not reach adult levels until the age of 9-11 years (Jeon, Hamid, Maurer, & Lewis, 2010; Semenov, Chernova, & Bondarko, 2000). Selective attention and oculomotor control are not mature until early adolescence (Aring, Gronlund, Hellstrom, & Ygge, 2007; Plude, Enns, & Brodeur, 1994). Hence, crowding can be regarded as a normal developmental phenomenon. However, which amount of crowding is normal during development?

The antecedent for the present thesis was a clinical observation made by ophthalmologists: children with visual impairment seemed to experience stronger crowding effects than children with normal vision. Visual acuity for optotypes presented in a row (line acuity) was poorer than visual acuity for optotypes presented in isolation (single acuity). Crowding is related to reading speed (Jeon, et al., 2010; Pelli

et al., 2007), and difficulties with reading long words (Jacobson, Ek, Fernell, Flodmark, & Broberger, 1996). In addition, reading speed is often slower in children with visual impairment (see e.g. Bosman, 2006; Merrill et al., 2011). It could therefore be hypothesized that foveal crowding interferes with the ability (to learn) to read and reading rate and can thus have an adverse effect on the acquisition of academic skills. It is important to investigate crowding in visual impairment, because crowding poses a restraint on reading and object recognition. However, there is a scarcity of information on the relation between visual impairment and crowding (see Chapter 3 for a systematic review). This thesis strives to fill this gap.

In the following sections, the criteria for visual impairment according to the World Health Organization will be presented (WHO). Next, I will give an overview of the factors influencing the crowding phenomenon. Finally, I will present the outline of this thesis and the four main research themes that will be covered. It is important to note that this thesis focuses on the quantification of crowding, the identification of key factors associated with crowding, and an intervention to reduce crowding in children with visual impairment.

### **WHO criteria for visual impairment**

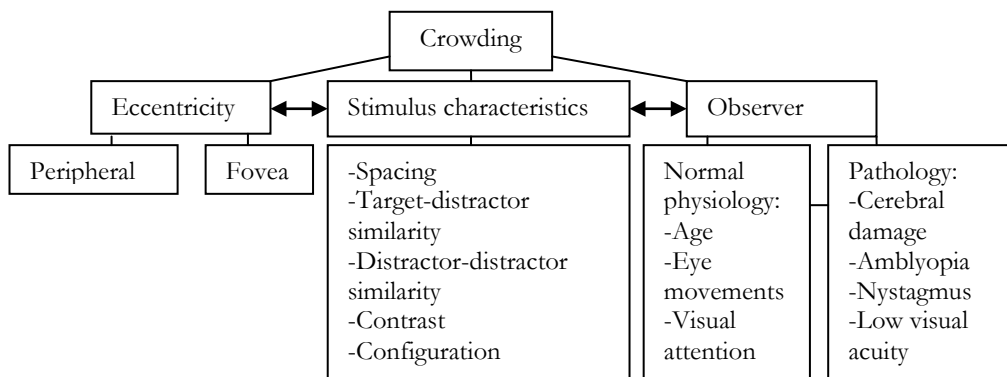
The WHO offers two classification systems. The first is the International Classification of Diseases (ICD) and the second is the International Classification of Functioning, Disability and Health (ICF). The ICD was founded in 1853 as an etiological framework for diagnostic classification. The ICF was added to the ICD system in 2002 and is a framework to describe the consequences of diseases in daily life. The International statistical Classification of Diseases and related health problems (ICD-10) defines having *low vision* as visual acuity in the best eye (with correction) less than 0.3 (20/70), but better than or equal to 0.05 ( $\geq 20/400$ ), and/or a corresponding visual field loss to less than  $20^\circ$  (WHO, 2010).

The majority of the studies presented in this thesis compare crowding effects between children with visual impairment and children with normal vision (Chapter 2, 3, 5-7). All children that were included had a normal developmental level. The first inclusion criterion for children with visual impairment was the impairment should have a peripheral origin (i.e., globe, retina, or anterior pathway). A second inclusion criterion for the children with visual impairment was visual acuity between 0.05 (20/400) and 0.40 (20/50) (that is, severe to mild visual impairment : Colenbrander, 2002). The inclusion criterion with regards to visual acuity in the children with normal vision was a (single) visual acuity of at least 0.80 or 20/25 (Kohler, 1973). Children with additional motor and/or intellectual impairments were excluded, because of the high

prevalence of additional impairments which might influence visual functioning (Mervis, Boyle, & Yeargin-Allsopp, 2002; Sonksen & Dale, 2002).

### Factors influencing crowding

Before one can investigate how a visual impairment contributes to crowding, it should be known which variables have already been related to crowding. There are three categories of variables (eccentricity, stimulus characteristics, and observer characteristics) that are known to influence crowding. However, it is not known how a visual impairment during childhood influences crowding effects. Figure 1.1 presents an overview of the variables that are known to influence the strength of crowding. Some of these factors are interrelated. In the following section, I will present the empirical evidence for the contribution of the variables presented in Figure 1.1. This section can be seen as a background model that can be used to interpret study results.

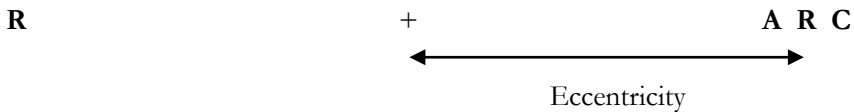


**Figure 1.1** Overview of related variables that influence the strength of crowding.

## 1. Eccentricity

### Peripheral vision

In 1970, the Dutch scientist Herman Bouma reported that, in the peripheral field of adults with normal vision, interaction effects between letters occurred over surprisingly large distances (Bouma, 1970). Bouma revealed a general rule, in line with his empirical findings, stating that the threshold distance between target and distractor scales linearly with target eccentricity: letters surrounding the target interfere with target recognition when they are placed at distances smaller than  $0.5 \times$  the eccentricity of the point of fixation to the target letter (see Figure 1.2). Thus, crowding becomes



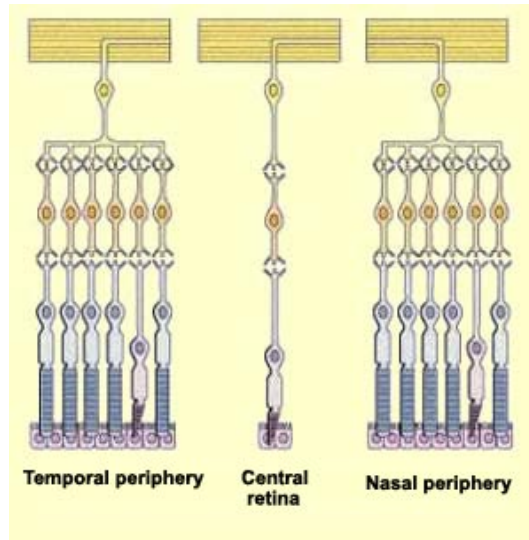
**Figure 1.2** Example of crowding. When fixating on the plus-sign in the middle, you will be able to identify the isolated letter on the left, but identifying the middle letter on the right is much harder because it is surrounded by the flanking letters.

stronger towards the visual periphery (Bouma, 1970; Strasburger, Harvey, & Rentschler, 1991; Toet & Levi, 1992). Research shows that Bouma’s constant (critical spacing is  $0.5\times$  eccentricity) should not be interpreted absolutely or as a single value, but that critical spacing (the minimal distance between target and distractor to avoid crowding) “depends on stimulus characteristics, task requirements, and attentional factors” (Whitney & Levi, 2011).

### Foveal vision

Crowding can also occur in foveal vision, the area subserving the central  $2^\circ$  of our visual field, and is reported to be much weaker than crowding in peripheral vision. This change might be related to the higher photoreceptor (cones) density in the retina and greater quality of form vision that pertains to the fovea than to the periphery (Strasburger, et al., 1991; Strasburger, Rentschler, & Juttner, 2011). Ganglion cells are the output cells of the retina, and each ganglion cell has a receptive field (i.e. portion of the visual field to which it responds). The average ratio of ganglion cells to photoreceptors in the retina is about 1:100. In foveal vision this ratio is 1:1, indicating that there is one ganglion cell for each cone receptor in the retina (see Figure 1.3). The ganglion to photoreceptor ratio shrinks linearly with eccentricity (McMahon, Lankheet, Lennie, & Williams, 2000). In normal adult foveal vision, crowding occurs over very small distances (3–5 minutes of arc: Danilova & Bondarko, 2007; Toet & Levi, 1992) or 4–6 minutes of arc (Flom, 1991) at the resolution limit, and the effect decreases if the target is slightly above the resolution limit (1 minute of arc: Danilova & Bondarko, 2007; Flom, 1991). Others mention that crowding effects are absent in foveal vision, yet at  $2^\circ$  from the fovea the crowding effect already is quite pronounced (Levi, 2008). Foveal crowding thus is a controversial term when it is used in the context of adult normal vision (Strasburger, et al., 1991). However, extensive crowding effects do occur in foveal vision of individuals with strabismic amblyopia (Danilova & Bondarko, 2007; Strasburger, et al., 1991).





**Figure 1.3** The ganglion cell to photoreceptor ratio in the fovea is 1:1, while the average ratio in the retina it is about 1: 100 (Figure obtained from <http://thebrain.mcgill.ca>, and published with permission).

## 2. Stimulus characteristics

### Spacing

Stimulus characteristics influence the strength of crowding effects. The first and most reported variable is element spacing (in peripheral vision: Bouma, 1970; Toet & Levi, 1992; in foveal vision: Haase & Hohmann, 1982; Hohmann & Haase, 1982; Rydberg, Ericson, Lennerstrand, Jacobson, & Lindstedt, 1999). Crowding effects become stronger when target and distractor are placed closer together (see Chapter 3 and 4). Contour interaction areas and critical spacing can be reduced after a period of perceptual learning (see Chapter 3 and Chapter 7).

### Target-distractor similarity

Second, crowding becomes stronger with increasing target-distractor similarity (Nazir, 1992; Whitney & Levi, 2011). This can be explained by the principle of target-distractor grouping. When target and distractor are highly dissimilar they are ungrouped and the target seems to “pop-out” (Scolari, Kohnen, Barton, & Awh, 2007; Whitney & Levi, 2011).

### **Distractor-distractor similarity**

Distractor-distractor similarity or “flanker-flanker grouping” is the third variable related to crowding. Crowding becomes weaker when distractors are more similar to each other and the target seems to be distinct (Whitney & Levi, 2011). Flanker-flanker grouping occurs in multi-element displays when elements are highly similar and distractors are grouped separately from the target. In contrast, when distractors are highly dissimilar they cannot be grouped, which decreases target salience, and increases crowding (Livne & Sagi, 2007; Livne & Sagi, 2010, see Chapter 5).

### **Contrast**

Contrast is the fourth variable that can influence the strength of crowding in both peripheral (Coates, Chin, & Chung, 2013) and foveal vision (Kothe & Regan, 1990b). Weaker contrast causes poorer resolution thresholds when it falls below a certain threshold, but reduces crowding effects (Coates, et al., 2013; Kothe & Regan, 1990b). That is, the difference between single acuity scores and line acuity scores is smaller for charts with lower contrast. Kothe and Regan evaluated the difference between high (96%), medium (11%), and low (4%) contrast Snellen charts in children aged 5-12 years and found weaker crowding effects for the low contrast charts than the high contrast charts. Possible explanations for these findings were: (i) weaker lateral interactions with lower contrast, and (ii) accuracy/steadiness of gaze control might be worse when contours close to the desired point of fixation are of high than of low contrast (Kothe & Regan, 1990b).

### **Configuration**

Fifth, configuration of the stimulus can also influence the strength of crowding. In peripheral vision, Toet and Levi found an elliptically shaped spatial interaction zone at 2.5°, 5°, and 10° eccentricity, with the long axis along the radial line connecting the fovea to the peripheral location of the target (Toet & Levi, 1992). In normal foveal vision, crowding effects seem to be stronger when targets are circumferentially surrounded by distractors than when they are surrounded by lateral distractors (Atkinson, Pimm-Smith, Evans, Harding, & Braddick, 1985 : see Chapter 5).

## **3. Observer characteristics**

### **A. Normal physiology**

#### **Age**

Age is an important observer characteristic that can predict the strength of crowding effects, because stronger crowding effects are to a certain degree typical of normal visual development. While single visual acuity is said to be mature around the age of 6 years (for a review see Simons, 1983), visual acuity measured with distractors

surrounding the target is still not mature at age 9 (Semenov, et al., 2000), or even age 11 (Jeon, et al., 2010). Thus, crowding in central vision seems to be a normal developmental phenomenon that can be explained by contour interaction (lateral masking), immature selective attentional mechanisms, and immature fixational eye movements/gaze instability (Jeon, et al., 2010; Kothe & Regan, 1990a; Norgett & Siderov, 2011 : see Chapter 2).

### **Eye movements**

Two types of eye movement control are of relevance in crowding: the ability to maintain stable fixation, and the ability to accurately move the eye from one element to another (fixational saccade: Flom, 1991). Kothe and Regan also underlined the importance of gaze selection and control on crowding in 4-11 year old children with normal vision (Kothe & Regan, 1990a). A number of studies using eye movement recordings also show less precise fine movement control in children than in adults (Kowler & Martins, 1982), and even show that fixational control does not reach adult accuracy until adolescence (Aring, et al., 2007).

### **Visual attention**

Attentional factors play a role in crowding (Chakravarthi & Cavanagh, 2009; Freeman & Pelli, 2007; Scolari, et al., 2007). Attention is the mechanism enabling us to select relevant information out of irrelevant noise (Carrasco, 2011). In peripheral crowding, attention can modulate critical spacing in crowded displays. This has been demonstrated by studies pre-cuing target location or using (colour) pop-out effects, which leads to smaller critical spacing (for a review see Whitney & Levi, 2011). In foveal vision, crowding can occur due to response competition between symbols and the target symbol has to be selected for discrimination. Interference control, or selective attentional mechanisms, have to be allocated to filter out the target from distractors (Bondarenko & Semenov, 2005; Jeon, et al., 2010; Norgett & Siderov, 2011; Semenov, et al., 2000).

## **B. Pathology**

### **Cerebral damage**

Cerebral damage can also influence the strength of crowding effects. Extensive crowding effects have been reported in children with cerebral visual impairment (CVI, see Jacobson, et al., 1996; Pike et al., 1994), and patients with posterior cortical atrophy (PCA, see Crutch & Warrington, 2007). The locus of damage varies for these patient groups. Neuroimaging studies in children with CVI reported parieto-occipital damage and damage to frontal areas of the brain (Pavlova, Bidet-Ildei, Sokolov, Braun, & Krageloh-Mann, 2009; Pavlova, Sokolov, & Krageloh-Mann, 2009). PCA is

associated with bilateral parieto-occipito-temporal atrophy and hypometabolism (Andrade et al., 2012; Delazer, Benke, Trieb, Schocke, & Ischebeck, 2006). These studies illustrate that extensive crowding can be part of the profile of far-reaching visuo-spatial functioning deficits in patients with CVI or PCA (see Chapter 3 for an overview on crowding ratios in children with CVI).

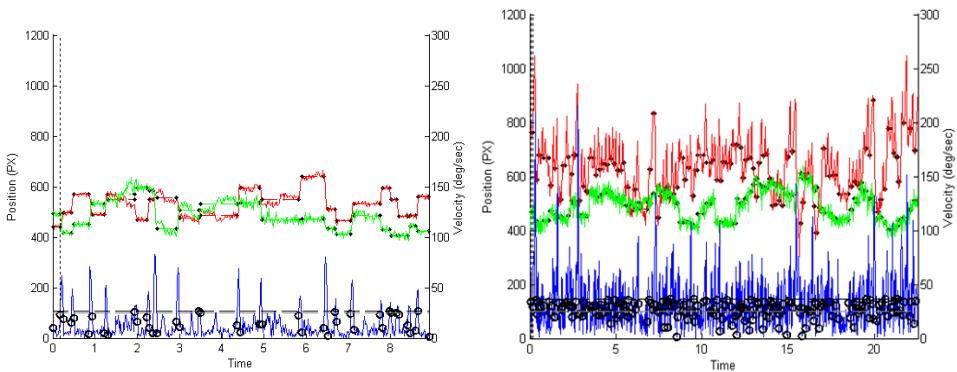
### **Amblyopia**

Amblyopia, defined as impaired visual acuity of one eye associated to cortical suppression of the inputs from that eye, demonstrates that peripheral disorders can induce altered low- and high-level visual processing as well as cortical brain reorganization (Cavezian et al., 2013). While crowding is only part of the profile in patients with CVI or PCA, crowding and impaired spatial resolution (in the suppressed eye) have been proposed to be the characteristic symptoms of amblyopia (Hussain, Webb, Astle, & McGraw, 2012). Strabismic amblyopia, that is amblyopia due to a turned eye, has been associated with extensive foveal crowding effects (Greenwood et al., 2012; Levi, 2008). Recent studies have reported that not only the amblyopic eye, but visual acuity of the fellow eye is also affected (Varadharajan & Hussaindeen, 2012). The prevalence of strabismus is considerably higher in children with visual impairment than in children with normal vision ( 1.5% in children with normal vision: Almeder, Peck, & Howland, 1990, 17% in idiopathic nystagmus, and 53% in albinism : Brodsky & Fray, 1997). Chapter 6 explores the association between amblyopia and mono- and binocular crowding in children with visual impairment.

### **Nystagmus**

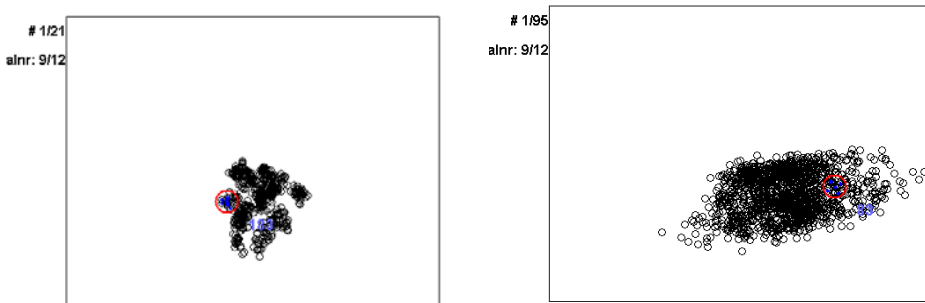
Infantile nystagmus is an involuntary, bilateral, conjugate oscillation of the eyes which is present at birth or develops within the first 6 months after birth (Abadi & Bjerre, 2002). It can occur in combination with an afferent visual defect such as albinism, congenital cataract or optic atrophy, or occurs without any visual or neurological impairment, in which case it is called 'idiopathic' nystagmus (Fu, Bilonick, Felius, Hertle, & Birch, 2011). Nystagmus is associated with large contour interaction areas (Chung & Bedell, 1995; Pascal & Abadi, 1995). Contour interaction is a type of spatial lateral masking which is often used as a synonym for crowding effects. According to Flom (1991) and others (Danilova & Bondarko, 2007) contour interaction is a much simpler phenomenon than crowding and can be seen as a component of crowding. While contour interaction involves a stationary eye, crowding requires eye movements in an array (Flom, 1991). The studies presented in this dissertation are the first to investigate the role of nystagmus on crowding (see Chapter 2 and 6). Nystagmus characteristics show large intersubject variability: nystagmus amplitudes range from 0.3-15.7°, nystagmus frequencies range from 0.5-8Hz (Abadi & Bjerre, 2002), and

peak velocities of the eye from 20-180°/s (Abadi & Worfolk, 1989). Chapter 6 investigates the association between nystagmus characteristics and crowding. Figure 1.4 displays eye movement velocity and X- and Y-coordinates of a child with normal vision and a child with nystagmus during a visual search task.



**Figure 1.4** The left panel displays oculomotor recordings of a 12-year-old girl with normal vision during visual search. The right panel displays recordings of a 12-year-old girl with ocular albinism and nystagmus performing the same trial. The blue line represents eye movement velocity, the red line the X- coordinate, and the green line the Y-coordinate.

Figure 1.5 displays raw fixation points of a child with normal vision and a child with nystagmus during a visual search task.



**Figure 1.5** The left panel displays raw fixation points of a 12-year-old girl with normal vision during the same visual search trial as displayed in Figure 1.4. The right panel displays the raw fixation points of a 12-year-old girl with ocular albinism and nystagmus.

### **Low visual acuity**

Finally, visual acuity or resolution capacity of the visual system has been mentioned as a variable related to crowding: visual acuity poorer than 20/60 has been associated with higher crowding ratios (Pike et al., 1994). This observation was made in a sample of 39 children with CVI. Twenty of these children also had impaired acuity (defined by the authors as visual acuity equal to or less than 20/60). This group had greater damage to optic radiation and/or occipito-parietal cortex than the group of children with normal or near-normal acuity, a greater part of the group showed neurodevelopmental deficits, and strabismus and optic atrophy were more common in this group. From this research it is not clear whether low visual acuity causes stronger crowding effects, but low visual acuity is associated with higher crowding ratios. Thus, there might be a relationship between foveal crowding effects and acuity, but analysis on a more detailed and fine-grained level shows that there are certain specific factors which are more predictive of crowding than acuity (such as nystagmus characteristics, the presence of strabismus, stimulus characteristics: see Chapter 2 and 6).

**Overview of the dissertation**

The present thesis focuses on the quantification and treatment of crowding effects in children with visual impairment. This section presents an outline of the content covered in the following chapters and the four main themes.

**Chapter 2** compares crowding ratios of 4-8 year old children with visual impairment and children with normal vision. In children with visual impairment the influence of nystagmus on crowding is investigated. Two questions are answered:

- Do crowding ratios differ between children with visual impairment and normal vision?*
- What is the influence of age and test design on crowding ratios?*

**Chapter 3** systematically reviews the literature on: (i) crowding ratios and contour interaction in children with normal vision, children and adults with visual impairment, and children with CVI, and (ii) interventions to reduce crowding. Two questions are addressed:

- Are there differences in the amount of (foveal) crowding between the three groups?*
- Is perceptual learning an effective method to reduce crowding ratios?*

**Chapter 4** compares the influence of two methods of magnification (magnifier versus large print), both applied in educational settings, on crowded task performance. Performance measures are compared for children working with a magnifier or large print. The main question is:

- Do children perform equally well with a magnifier as with large print?*

**Chapter 5** evaluates the influence of element spacing, configuration, attentional factors, and oculomotor control on visual search performance of 6-8 year old children with visual impairment and children with normal vision. Three questions are answered:

- Do children with VI+nys show poorer performance than children with NV on visual search tasks with small element spacing?*
- Do children with VI show weaker performance than children with NV in the matrix configuration with homogeneous distractors?*
- Do children with VI show a disproportionately poor search performance on serial tasks compared to children with NV?*

**Chapter 6** compares interocular acuity differences, mono- and binocular crowding ratios, and binocular summation ratios in 4-8 year old children with albinism, infantile nystagmus syndrome, and children with normal vision. This study also evaluates the contribution of five predictors on mono- and binocular crowding ratios: nystagmus

amplitude, nystagmus frequency, strabismus, astigmatism, and anisometropia. Three questions are answered:

- Do groups show dissimilar amounts of interocular acuity differences?
- Do crowding ratios differ between groups?
- Do binocular summation ratios differ between groups?

**Chapter 7** describes the prospects of 6-weeks of training on the reduction of crowding ratios and improvement of near visual acuity measures in children with visual impairment. Three questions are answered:

- Are crowding ratios higher and is baseline performance on the training task poorer for children with visual impairment than children with normal vision?
- Is the experimental perceptual learning task most effective in reducing crowding ratios and improving near visual acuity?
- Does training transfer to untrained visual functions, such as NVA?
- Are improvements larger for 7-9 year-old children than 4-6 year-old children?



**Main themes covered in this thesis**

As can be read in the preceding section, each chapter contains several research questions. These questions are quite specific and fall within four main research themes:

1. Crowding ratios
2. Stimulus characteristics
3. Magnification and crowding
4. Intervention: Reduction of crowding by perceptual learning

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Crowding in central vision  
in normally sighted and  
visually impaired children  
aged 4 to 8 years:  
The influence of age and  
test design

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**ABSTRACT**

**Background/aims:** To investigate crowding ratios in children with a visual impairment due to ocular disease (n=58) and normally sighted children (n=75) aged 4 to 8 years using several variants of two clinically available tests with different optotype spacing (fixed or proportional to the optotype size).

**Methods:** Crowding ratios, calculated by dividing the single acuity by the linear acuity, were measured binocularly with the C-test and the LH line chart. Ratios >1.00 indicate crowding.

**Results:** The charts with fixed spacing revealed significantly higher crowding ratios for visually impaired children than normally sighted children (both for measurements at 40cm and 5m). The age related reduction of the crowding ratios seen in normally sighted children when tested with near vision charts with fixed spacing, was not present in the visually impaired group. Visually impaired children with nystagmus showed higher crowding ratios than visually impaired children without nystagmus. The chart with proportional inter-symbol-spacing did not reveal differences between the normally sighted and visually impaired children; nor did it show group, age or nystagmus effects.

**Conclusion:** Visually impaired children showed higher crowding ratios than normally sighted children when measured with charts with fixed inter-symbol-spacing. This study illustrates that test design and target/flanker interference as a manifestation of crowding are critical issues to bear in mind when assessing crowding ratios in children.



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## INTRODUCTION

Crowding is generally defined as the deleterious influence of nearby contours on object recognition (Levi, 2008), a bottleneck in perception or separation difficulty (Stuart & Burian, 1962). It can be seen as a developmental phenomenon, as crowding effects are larger in children than in adults (Jeon, et al., 2010). Past studies have delivered evidence for foveal crowding in normally sighted (NS) young children (Atkinson, Pimm-Smith, Evans, Harding, & Braddick, 1985; Jeon, et al., 2010; Kothe & Regan, 1990a), children and adults with strabismus (Hohmann & Haase, 1982; Rydberg, et al., 1999), adults with congenital nystagmus (Chung & Bedell, 1995; Pascal & Abadi, 1995; Simmers, Gray, & Winn, 1999) and visually impaired (VI) adults with ocular disease (Pardhan, 1997).

Several factors have been mentioned to explain the strength of this phenomenon: age (all the above studies), contrast (Kothe & Regan, 1990b), fixation stability (Kothe & Regan, 1990a; Wolford & Chambers, 1984), nystagmus (Chung & Bedell, 1995; Pardhan, 1997; Pascal & Abadi, 1995), central scotomas (Pardhan, 1997), configuration of stimuli (Atkinson et al., 1985), amblyopia (Hohmann & Haase, 1982), maturation of retinal factors (cone packing density), maturation of V1 (synaptic density is mature at 11 years: Jeon et al., 2010), and the maturation of selective attention mechanisms (Flom, Heath, et al., 1963; Wolford & Chambers, 1984).

In the past, two studies have been published about the degree of crowding in NS and VI children (Rydberg, et al., 1999) and NS and VI adults (Pardhan, 1997) measured with a proportional chart. These studies have reported contrasting findings. The first (Rydberg, et al., 1999) found no differences between NS and VI children and the second (Pardhan, 1997) did find higher crowding ratios for VI than NS adults. The majority of VI adults had eccentric fixation because of central scotomas, whereas the children in the study by Rydberg et al. (1999) had conditions which did not lead to eccentric fixation. However, the study by Rydberg et al. was based on a relatively small group of VI children with no specification of the presence of nystagmus (which is known to be related to larger contour interaction areas: Chung & Bedell, 1995; Pascal & Abadi, 1995; Simmers et al., 1999).

The goal of this study was to measure crowding ratios in NS and VI children with a variety of visual charts. We predicted a higher crowding ratio for VI children than for NS children (group effect), mainly because of the presence of fixation instability in the VI group. In addition we expected an age related decline of the crowding ratio in both groups (age effect), because of more mature oculomotor and interference control. Third, the presence of nystagmus was expected to influence the crowding ratio in the VI group, because this group in particular experiences most fixation instability. Finally, we expected that all the above mentioned effects would be stronger for the charts

with fixed spacing compared to the proportional charts, because below the 20/20 acuity line, the symbols are more closely spaced on charts with fixed spacing compared to charts with proportional spacing.

## MATERIALS AND METHODS

### Participants

Crowding ratios were measured in 75 NS children and 58 VI children. Inclusion criteria were: age 4 to 8 years, normal developmental level,  $\geq 36$  weeks of gestation, and birth weight of  $\geq 3000$  grams. Children with nystagmus, strabismus or refractive errors were included in the VI group. In the VI group the distance visual acuity was 20/50 or worse. Exclusion criteria were intellectual and/or motor impairments and the presence of central scotomas. Information regarding gestational age and the presence of additional impairments was obtained from medical records. NS children had distance acuities of 20/25 or better. NS children were included from regular primary schools in the Netherlands and VI children were included from client databases of all Dutch vision rehabilitation centres. The project was approved by an accredited Medical Review Ethics Committee (CMO-Arnhem Nijmegen) and the protocol adhered to the tenets of the Declaration of Helsinki.

Table 2.1 presents the characteristics of both groups (gender, age and mean near and distance visual acuity). The supplementary file presents the diagnosis and distance visual acuity for children in the VI group.

**Table 2.1** *Characteristics of the normally sighted and visually impaired group (M, (SD)).*

	Age in years											
	4		5		6		7		8		Total	
	NS	VI	NS	VI	NS	VI	NS	VI	NS	VI	NS	VI
No.	8	8	12	13	18	11	23	13	14	13	75	58
Female	6	1	8	5	14	3	9	3	8	3	46	15
NVA*	-.01 (.12)	.81 (.25)	-.08 (.07)	0.68 (.25)	-.12 (.09)	.56 (.25)	-.15 (.08)	.35 (.11)	-.17 (.11)	.52 (.14)	-.12 (.10)	.56 (.25)
DVA* *	-0.02 (.08)	0.87 (.22)	-.02 (.05)	0.69 (.20)	-.06 (.03)	.71 (.24)	-.07 (.02)	.61 (.26)	-.05 (.06)	.59 (.15)	-.04 (.06)	.68 (.23)

\* Near visual acuity (NVA) as measured with LH single optotypes (LogMAR values).

\*\* Distance Visual Acuity (DVA) measured with E-gratings at 6m (LogMAR values).

### Ophthalmological examination

All children (VI and NS) were examined ophthalmologically. Distance visual acuity was measured monocularly and binocularly with the E-chart (Taylor, 1978) at 6 m with 100% inter-symbol-spacing (ISS), and with the C-test (Hohmann & Haase, 1982) at 5 m. Near visual acuity was assessed at 40cm binocularly with the proportional LH

line charts (Hyvarinen, Nasanen, & Laurinen, 1980), the C-test (Hohmann & Haase, 1982) and an equivalent LH-version of the C-test which was created by the authors (see Figure 2.1-3 for examples of the charts). The charts were administered in a room with ambient lighting of 76-148 cd/m<sup>2</sup>. Children had to identify the first five symbols per row, which were pointed out with a pencil, and could progress to the next line on the acuity chart if they correctly identified three or more of the five symbols. If there were fewer than five symbols on a row, children could progress if they could correctly identify at least half of symbols. NS children were measured at 5m distance. In the VI group, when LC acuity was below 0.16, the distance was reduced to 2.5m (3.3' ISS for the crowded chart) and 1.25m (4.1' ISS).

Objective refraction was obtained after cycloplegia and if necessary the spectacle correction was prescribed or changed before the experiment started. All children with glasses had to wear them during the entire study.

### **Crowding ratios**

Crowding ratios were calculated by dividing the single acuity value (as measured by the uncrowded version of the C-test) with the crowded acuity value. Six different crowding ratios were calculated. At 40 cm distance:

-C-test ratio: uncrowded C-test decimal score divided by the crowded C-test decimal score;

-LH version of C-test ratio: uncrowded C-test (LH version) decimal score divided by the crowded C-test decimal score (LH version);

-LH<sub>25%</sub>ratio: uncrowded C-test (LH version) decimal score divided by the LH line 25% crowding decimal score;

-LH<sub>50%</sub>ratio: uncrowded C-test (LH version) decimal score divided by the LH line 50% crowding decimal score;

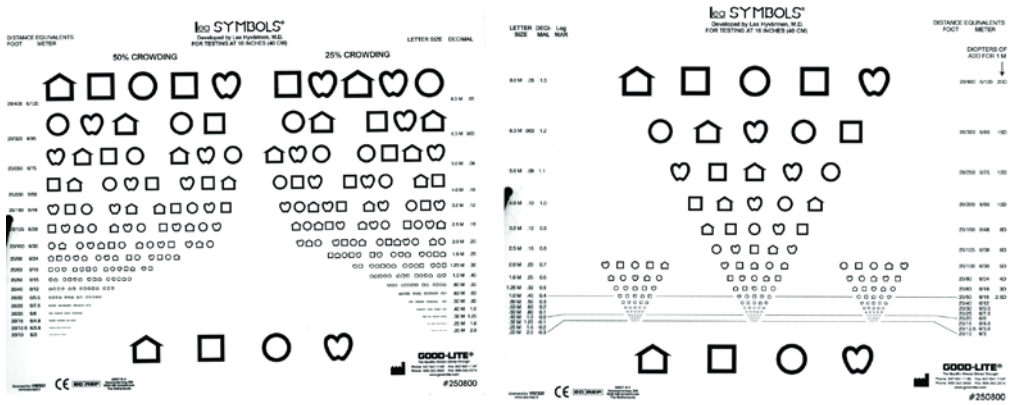
-LH<sub>100%</sub>ratio: uncrowded C-test (LH version) decimal score divided by the LH line 100% crowding decimal score.

At 5m distance:

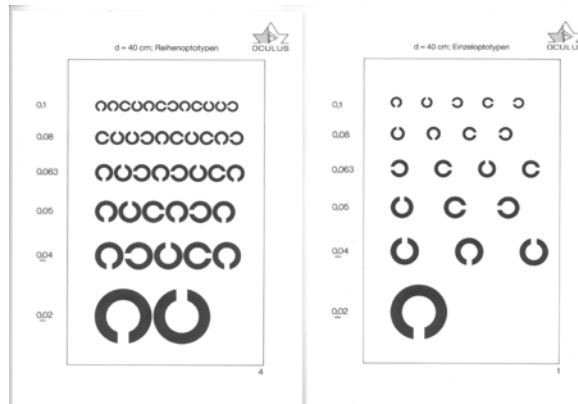
-C-test ratio: uncrowded C-test decimal score divided by the crowded C-test decimal score.

### **Statistical analysis**

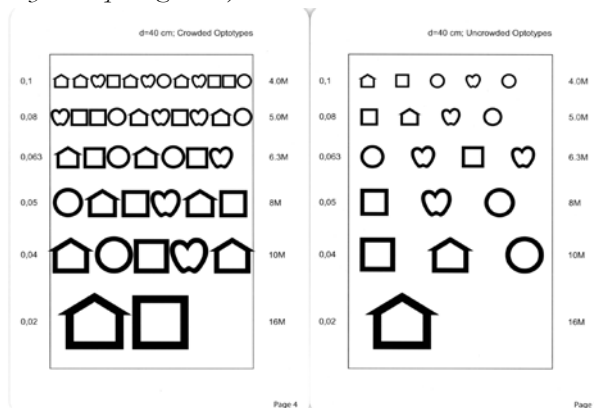
A general linear model was applied to the data in order to investigate the influence of age and group on the crowding ratios. The first step was to conduct a single ANOVA with age (5 levels: 4, 5, 6, 7 and 8 years old) and group (2 levels: VI and NS) as between-subjects factors, and crowding ratios (6 levels: the six different crowding ratios described above) as within-subjects factor. Six post-hoc ANOVAs were performed, one on each of the six crowding ratios. If this then revealed an age x



**Figure 2.1** Example of LH line proportional acuity chart with inter-symbol-spacing of 50% and 25%, respectively, on the left chart and 100% on the right chart.



**Figure 2.2** Example of the C-test with a crowded page (inter-symbol-spacing of 2.6') and an uncrowded page (inter-symbol-spacing  $\geq 30'$ ).



**Figure 2.3** Example of the LH version of the C-test with a crowded page (inter-symbol-spacing 2.6') and an uncrowded page (inter-symbol-spacing  $\geq 30'$ ).

group interaction effect, a one-way ANOVA was performed to examine the effect of age in the NS and VI group separately. If this resulted in a significant effect, a post-hoc Bonferroni test was performed to find out which ages differed from each other significantly. To investigate whether groups differed from each other, a one-way ANOVA was conducted with age as a covariate and group as between-subjects factor. Finally, the last step was to investigate with a one-way ANOVA whether there was a difference within the VI group between children without nystagmus, and VI children with nystagmus (age was entered as a covariate). The LH single decimal acuity score at 40cm was entered as a covariate to rule out that differences in crowding ratios were purely caused by acuity differences. There were 5 children with strabismus. The average crowding ratios in this group are presented separately.

## RESULTS

There was a significant 3-way interaction in the first ANOVA between age, group and crowding ratios,  $F(20, 605)=1.61, p=.045$ , partial  $\eta^2=.051$ . The single ANOVA also showed that there was a significant difference between the six crowding ratios,  $F(5, 605)=59.57, p=.000$ , partial  $\eta^2=.330$  (see Table 2.2). There was a significant interaction effect between the crowding ratios and group,  $F(5, 605)=5.12, p=.000$ , partial  $\eta^2=.041$ . There was a significant interaction effect between the crowding ratios and age,  $F(20, 605)=2.82, p=.000$ , partial  $\eta^2=.051$ . Between-subjects analysis showed that there was a significant difference between the crowding ratios measured in NS children and VI children,  $F(1, 121)=12.04, p=.000$ , partial  $\eta^2=.090$ . There was no overall effect of age on the crowding ratios,  $F(4, 121)=1.80, p=.133$ , partial  $\eta^2=.056$ . There was an interaction effect between group and age,  $F(4, 121)=4.141, p=.004$ , partial  $\eta^2=.120$ .

The significant 3-way interaction was explored further by performing six post-hoc ANOVAS, one on each of the six crowding ratios (see Table 2.2). Post hoc analysis revealed that there was a significant group x age interaction effect on the C-test ratio,  $F(4, 123)=6.04, p=.000$ , partial  $\eta^2=.164$ . There was a significant group x age interaction effect on the LH-version of the C-test ratio,  $F(4, 123)=4.64, p=.002$ , partial  $\eta^2=.131$ . The interaction effect for the LH<sub>25%</sub>ratio was not significant,  $F(4, 121)=2.11, p=.084$ , partial  $\eta^2=.065$ . There was no effect of age for the LH<sub>25%</sub>ratio,  $F(4, 121)=0.57, p=.684$ , partial  $\eta^2=.019$ . Neither was there an effect of group for the LH<sub>25%</sub>ratio,  $F(1, 121)=0.20, p=.652$ , partial  $\eta^2=.002$ . The interaction effect for the LH<sub>50%</sub>ratio was significant,  $F(4, 121)=2.82, p=.028$ , partial  $\eta^2=.085$ . The interaction effect for the LH<sub>100%</sub>ratio was not significant,  $F(1, 121)=1.426, p=.229$ , partial  $\eta^2=.045$ . There was no effect of age for the LH<sub>100%</sub>ratio,  $F(4, 121)=0.57, p=.684$ , partial  $\eta^2=.019$ . Again, neither was there an effect of group for the LH<sub>100%</sub>ratio,  $F(1, 121)=0.05, p=.822$ , partial  $\eta^2=.822$ . The C-test ratio at 5m distance showed no group x age interaction,  $F(4, 121)=0.47, p=.759$ , partial  $\eta^2=.015$ . There was an effect of age on the C-test ratio,

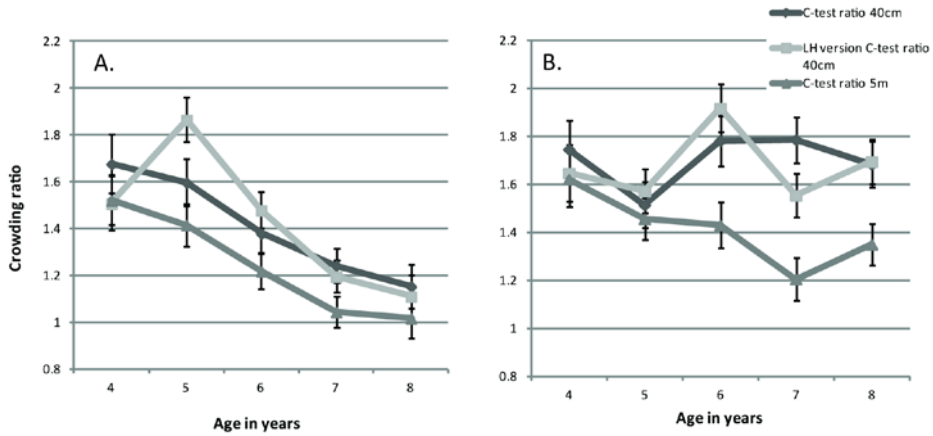
**Table 2.2** Outcome different crowding ratios (*M*, (*SD*)).

	Crowding ratios		Age × group interaction	Age effect		Differences between ages		Group effect
	NS	VI		NS	VI	NS	VI	
<b>Near (40cm)</b>								
C-test ratio	1.39 (0.42)	1.67 (0.38)	Yes***	Yes***	No	5>6-8, 6>7-8	n.a.	Yes***
LH version C-test ratio	1.36 (0.33)	1.70 (0.38)	Yes**	Yes***	No	4>7-8, 5>7-8	n.a.	Yes***
LH 25% ratio	1.16 (0.41)	1.20 (0.36)	No	No	No	n.a.	n.a.	No
LH 50% ratio	1.09 (0.35)	1.18 (0.42)	Yes*	No	No	n.a.	n.a.	No
LH 100% ratio	1.09 (0.34)	1.11 (0.37)	No	n.a.	n.a.	n.a.	n.a.	No
<b>Distance (5m)</b>								
C-test ratio	1.17 (0.27)	1.39 (0.39)	No	Yes***		4>6-8, 5>7		Yes**

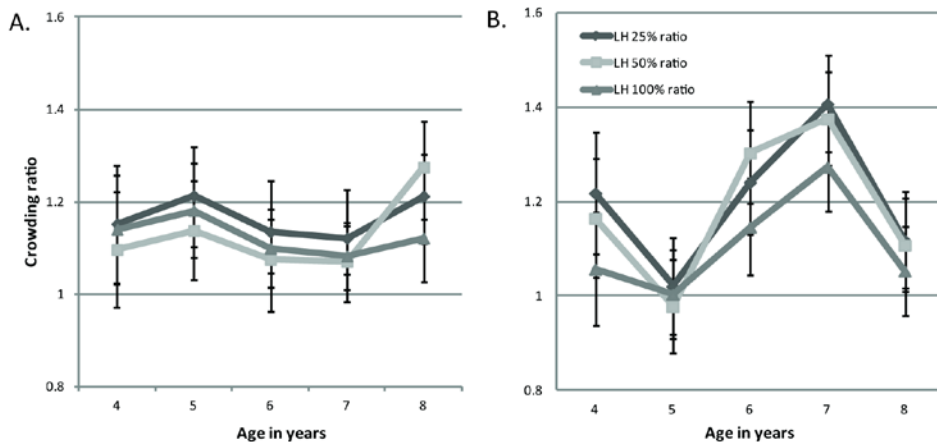
\*  $p < .05$ , \*\*  $p < .01$ , \*\*\*  $p < .001$ .

$F(4, 121)=7.04$ ,  $p=.000$ , partial  $\eta^2=.189$ . Post-hoc Bonferroni analysis showed that the 4 year olds showed significantly higher C-test ratios at 5m than the 6 to 8 year olds and the 5 year olds showed significantly higher ratios than the 7 year olds. The VI children showed significantly higher C-test ratios at 5m than NS children,  $F(1, 121)=12.71$ ,  $p=.001$ , partial  $\eta^2=.095$  (see Figure 2.4). Visually impaired children show higher crowding ratios and, in contrast with normally sighted children, show no age-related reduction of the fixed crowding ratio.

Because there were age x group interaction effects for the C-test ratio, the LH version of the C-test ratio and the LH<sub>50%</sub>ratio, one-way ANOVAS were conducted. In the NS group, there was an age related reduction of the C-test crowding ratio,  $F(4, 70)=10.80$ ,  $p=.000$ , partial  $\eta^2=.382$ . A post-hoc Bonferroni test was performed. The 5 year old NS children showed a significantly higher C-test ratio than the 6, 7 and 8 year olds (see Figure 2.4). The VI children showed no age related reduction of the C-test crowding ratio,  $F(4, 53)=1.81$ ,  $p=.140$ , partial  $\eta^2=.121$  (see Figure 2.4). Accordingly, the LH version of the C-test showed an age related reduction of the crowding ratio in the NS group,  $F(4, 70)=7.44$ ,  $p=.000$ , partial  $\eta^2=.298$ . The 4, and 5 year old NS children showed higher crowding ratios on the LH version of the C-test than the 7, and 8 year olds (see Figure 2.4). There was no age related reduction of the LH version of the C-test ratio in the VI group,  $F(4, 53)=1.091$ ,  $p=.371$ , partial  $\eta^2=.076$ . The LH<sub>50%</sub>ratio did not show an age effect for the NS group,  $F(4, 68)=1.03$ ,  $p=.400$ , partial  $\eta^2=.057$  (see Figure 2.5). Nor did it in the VI group,  $F(4, 53)=1.95$ ,  $p=.116$ , partial  $\eta^2=.128$ . Group effects were also further investigated for the C-test ratio, the LH version of the C-test



**Figure 2.4** Panel A shows fixed crowding ratios as a function of age in years for normally sighted children. Diamonds represent the C-test ratio at 40 cm, the squares represent the LH version of the C-test ratio at 40cm and triangles represent distance C-test ratio at 5 m. Panel B shows fixed crowding ratios for visually impaired children. Other details as in Panel A.



**Figure 2.5** Proportional crowding as a function of age in normally sighted children (Panel A) and visually impaired children (Panel B). Diamonds represent the LH 25% ratio, squares represent LH 50% ratio, and triangles represent LH 100% ratio. The proportional charts measure no differences in crowding ratios between groups or ages.

ratio and the LH<sub>50%</sub>ratio with age entered as a covariate (see Table 2.2). VI children showed a C-test ratio of 1.67 (SD=0.38) and the NS children showed a significantly lower ratio of 1.39 (SD=0.42),  $F(1, 130)=16.39$ ,  $p=.000$ , partial  $\eta^2=.112$ . The VI children showed a LH-version of the C-test ratio of 1.70 (SD=0.38) and the NS children scored a significantly lower ratio of 1.36 (SD=0.33),  $F(1, 130)=29.20$ ,  $p=.000$ ,

partial  $\eta^2=.183$ . The VI children showed a LH<sub>50%</sub>ratio of 1.18 (SD=0.42) and the NS children showed a ratio of 1.09 (SD=0.35). This difference was not significant,  $F(1, 128)=1.99, p=.160$ , partial  $\eta^2=.015$ .

The effect of nystagmus was calculated for the six crowding ratios (see Table 2.3). VI children with nystagmus ( $n=38$ ) displayed a ratio of 1.78 (SD=0.39) on C-test at near and VI children without nystagmus ( $n=20$ ) showed a crowding ratio of 1.47 (SD=0.26),  $F(1,54)=11.48, p=.001$ , partial  $\eta^2=.175$ . The VI children with nystagmus showed a ratio of 1.78 (SD=0.40) for the LH version of the C-test and the VI children without nystagmus showed a crowding ratio of 1.54 (SD=0.28),  $F(1,54)=10.33, p=.002$ , partial  $\eta^2=.161$ . The five children with strabismus (3 also had nystagmus) showed an average C-test crowding ratio of 1.60 (SD=0.55) and 1.54 (SD=0.30) on the LH version of the C-test. The VI group with nystagmus had an average distance C-test crowding ratio of 1.51 (SD=.40) and those without nystagmus presented with a ratio of 1.17(SD=.26),  $F(1,54)=15.12, p=.000$ , partial  $\eta^2=.219$ . Strabismic children showed an average ratio of 1.32 (SD=.49). The charts with proportional spacing did not reveal any significant differences between VI children without nystagmus and VI children with nystagmus (see Table 2.3).

**Table 2.3** *Influence nystagmus on crowding ratios within the visually impaired group.*

	VI without nystagmus (n=20)	VI with nystagmus (n=38)	Differences between groups
NVA LogMAR(LH single 40cm)	0.48 (0.19)	0.60 (0.26)	
<b>Near (40cm)</b>			
C-test ratio	1.47 (0.26)	1.78 (0.39)	Yes**
LH version C-test ratio	1.54 (0.28)	1.78 (0.40)	Yes**
LH 25% ratio	1.11 (0.22)	1.24 (0.41)	No
LH 50% ratio	1.12 (0.28)	1.22 (0.47)	No
LH 100% ratio	1.07 (0.29)	1.13 (0.41)	No
<b>Distance (5m)</b>			
C-test ratio	1.17 (0.26)	1.51 (0.40)	Yes***

\*  $p<.05$ , \*\* $p<.01$ , \*\*\* $p<.001$ .

## DISCUSSION

### Visual impairment and crowding

Our first hypothesis was that there would be higher crowding ratios for VI children than NS children (group effect). This hypothesis was confirmed when using the charts with fixed ISS. Because 12 children in the VI group were measured at a closer distance (and spacing is larger) than the prescribed testing distance of 5 m, the results of this part of the study are, if anything, underestimating the crowding effects in the VI



group. One explanation that can account for the higher crowding ratios found in VI children is that the C-test with its fixed ISS evoked more crowding at the lower acuity range of the chart than the proportional charts, because relative ISS is smaller in this range (Haase, 1993). However, this reason does not sufficiently explain the differences in results between charts. NS children still showed significantly higher ratios when measured with the fixed charts in comparison with the proportional LH charts. This is a curious finding, because spacing was smaller for NS children on the higher acuity range of the proportional chart (from 1.00 decimal acuity onwards, spacing is 2.5' and smaller). A second explanation for the higher crowding ratios found in VI children, is that the children confuse a flanking optotype with the target optotype. It was observed that they often mistakenly named the optotype on the left or right side of the target. When subjects report a flanking symbol rather than a target symbol, this can be seen as a sign of crowding (Whitney & Levi, 2011). This phenomenon indicates selection problems. Positional uncertainty due to inaccurate short fixations might be an explanation. Fixational eye movements in NS children are not mature until late adolescence (Luna, Velanova, & Geier, 2008). But it is conceivable that VI children make more inaccurate fixations than NS children.

### **Age and crowding**

The second hypothesis of an age-related reduction of crowding effects was partially confirmed when looking at the crowding ratio that was measured when using fixed ISS. The age-related reduction of crowding ratio was present only in the NS group. The absence of an age-related decline on the crowding ratio in the VI group, is also a well-known finding in children with amblyopia (Hohmann & Haase, 1982). The proportional LH chart did not measure an age-related reduction of crowding. This is in line with the findings of Rydberg et al. (1999). Older children had higher acuity values, as visual acuity is still improving within the age range of our sample, and crowding effects are known to be larger in children up to at least eleven years of age compared to adults (Jeon et al., 2010).

### **Nystagmus and crowding**

In accordance with previous studies in adults (Chung & Bedell, 1995; Pascal & Abadi, 1995; Simmers et al., 1999), crowding ratios in VI children with nystagmus were higher than crowding ratios in VI children without nystagmus. In the current study this finding was present in the near and distance visual acuity charts with fixed ISS. It is highly plausible that children with nystagmus were not able to fixate long enough to decipher the small closely spaced symbols when presented in a row. A corroborating observation is that NS children were fixating longer when symbols were crowded. The near visual acuity chart with proportional ISS did not reveal this effect. Again, possible

explanations for this difference are test design and a smaller degree of target-flanker interference (substitution phenomenon) during proportional measurements.

### **Test design**

Only with the charts with fixed ISS did we find differences between groups, ages and the VI children with and without nystagmus. Children might have reached higher acuity values on the proportional chart because this chart has a maximum of four or five characters standing next to each other. This is a difference when comparing it to the C-test design with fixed spacing, where twelve characters are presented on each line for acuities 0.10 (20/200) and better. Thirteen of 58 VI children showed crowded acuities below 0.10. However, their crowding ratios did not differ from those with acuities 0.10 and better. Having more characters within the visual span increases the severity of interference.

### **CONCLUSION**

The present study is the first to compare crowding ratios calculated from different charts, in normally sighted children and visually impaired children between 4 and 8 years of age. Results show that inter-symbol-spacing and test design (fixed or proportional) have a substantial influence on crowding ratios. Charts with fixed inter-symbol-spacing generally measure higher crowding ratios and seem to be more sensitive in measuring age-related changes in the size of the crowding ratio. Because of the different outcomes measured with different charts, careful documentation and reporting of testing conditions, including the inter-symbol-spacing, is recommended to improve interpretation. This study shows that when measured with a chart with fixed inter-symbol-spacing, visually impaired children show higher crowding ratios than normally sighted children. The age related reduction of the crowding ratio seen in normally sighted children when tested with charts with fixed spacing, was not present in visually impaired children. Finally, visually impaired children with nystagmus showed higher crowding ratios than children without nystagmus. This outcome is of great importance, because the higher crowding ratios may affect daily activities such as reading. This issue deserves further investigation.

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<b>Supplement.</b>		<i>Types of visual impairment in VI group and distance visual acuity.</i>			
<b>Child</b>	<b>Age</b>	<b>VA*</b>	<b>Primary diagnosis</b>	<b>Nystagmus</b>	<b>Amblyopia</b>
110	4	0.20	Congenital Stationary Night Blindness		
122	4	0.20	Congenital Stationary Night Blindness	+	
124	4	0.24	Juvenile X-linked retinoschisis		
142	4	0.20	Congenital nystagmus	+	
144	4	0.12	Albinism	+	
145	4	0.06	Albinism	+	
150	4	0.08	Albinism	+	
158	4	0.10	Achromatopsia	+	
105	5	0.06	Congenital cataract (aphakia)		
113	5	0.24	Juvenile X-linked retinoschisis		
118	5	0.36	CSNB		
120	5	0.06	Achromatopsia	+	
125	5	0.24	Juvenile X-linked retinoschisis		
130	5	0.20	Albinism	+	
134	5	0.12	Albinism	+	+ (Strab.)
138	5	0.20	Albinism	+	
143	5	0.24	Congenital nystagmus	+	
146	5	0.25	Juvenile X-linked retinoschisis		
152	5	0.20	Hypermetropia (>4 D)		+ (Strab.)
161	5	0.24	Retinitis Pigmentosa		
172	5	0.20	Congenital nystagmus	+	
107	6	0.36	Hypermetropia (>4D)	+	
116	6	0.08	Albinism	+	
117	6	0.12	Albinism	+	
123	6	0.36	Albinism, myopia >6D	+	
132	6	0.18	Myopia (high>6D)	+	
136	6	0.36	Congenital nystagmus	+	
141	6	0.12	Congenital cataract (aphakia)	+	
149	6	0.24	Congenital nystagmus	+	
156	6	0.15	Congenital glaucoma		
160	6	0.36	Hypermetropia (>4D)		+ (Strab.)
165	6	0.12	Congenital nystagmus	+	
101	7	0.12	Albinism	+	
103	7	0.24	Congenital nystagmus	+	
119	7	0.36	Albinism	+	
121	7	0.36	Albinism, myopia (>6D)		
126	7	0.36	Congenital nystagmus	+	+ (Strab.)

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127	7	0.36	Albinism		
133	7	0.30	Cone dystrophy, myopia (>6D)		
135	7	0.12	Congenital glaucoma		
139	7	0.36	Papildysplasia	+	+ (Strab.)
140	7	0.36	Corneal opacities		
147	7	0.36	Congenital Stationary Night Blindness		
170	7	0.40	Myopia (>6D)		
174	7	0.20	Albinism	+	
109	8	0.18	Congenital cataract (aphakia)	+	
112	8	0.36	Congenital nystagmus	+	
114	8	0.24	Albinism	+	
115	8	0.30	Cone dystrophy, myopia (>6D)		
131	8	0.24	Congenital Stationary Night Blindness	+	
154	8	0.30	Congenital Stationary Night Blindness	+	
159	8	0.20	Albinism	+	
163	8	0.24	Juvenile X linked retinoschisis	+	
164	8	0.24	Albinism	+	
167	8	0.12	Congenital Stationary Night Blindness	+	
168	8	0.36	Congenital nystagmus	+	
169	8	0.40	Aniridia	+	
175	8	0.36	Coloboma irides		

\* dec. VA as measured with E-gratings (distance acuity).

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A systematic review on  
'foveal crowding' in  
visually impaired children  
and perceptual learning as  
a method to reduce  
crowding

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## ABSTRACT

**Background:** This systematic review gives an overview of foveal crowding (the inability to recognize objects due to surrounding nearby contours in foveal vision) and possible interventions. Foveal crowding can have a major effect on reading rate and deciphering small pieces of information from busy visual scenes. Three specific groups experience more foveal crowding than adults with normal vision (NV): 1) children with NV, 2) visually impaired (VI) children and adults and 3) children with cerebral visual impairment (CVI). The extent and magnitude of foveal crowding as well as interventions aimed at reducing crowding were investigated in this review. The twofold goal of this review is: [A] to compare foveal crowding in children with NV, VI children and adults and CVI children and [B] to compare interventions to reduce crowding.

**Methods:** Three electronic databases were used to conduct the literature search: PubMed, PsycINFO (Ovid), and Cochrane. Additional studies were identified by contacting experts. Search terms included visual perception, contour interaction, crowding, crowded, and contour interactions.

**Results:** Children with normal vision show an extent of contour interaction over an area 1.5-3× as large as that seen in adults NV. The magnitude of contour interaction normally ranges between 1-2 lines on an acuity chart and this magnitude is even larger when stimuli are arranged in a circular configuration. Adults with congenital nystagmus (CN) show interaction areas that are 2× larger than those seen adults with NV. The magnitude of the crowding effect is also 2× as large in individuals with CN as in individuals with NV. Finally, children with CVI experience a magnitude of the crowding effect that is 3× the size of that experienced by adults with NV.

**Conclusions:** The methodological heterogeneity, the diversity in paradigms used to measure crowding, made it impossible to conduct a meta-analysis. This is the first systematic review to compare crowding ratios and it shows that charts with 50% interprototype spacing were most sensitive to capture crowding effects. The groups that showed the largest crowding effects were individuals with CN, VI adults with central scotomas and children with CVI. Perceptual Learning seems to be a promising technique to reduce excessive foveal crowding effects.



## BACKGROUND

Visual crowding is a behavioral phenomenon that occurs when identification of an object is seriously undermined by the presence of flankers (Bouma, 1970). Classically, the phenomenon is thought to be caused by contour interaction, attentional factors and/or inaccurate eye movements (Flom, 1991). The magnitude of the crowding phenomenon or contour interaction in foveal vision (comprising only two degrees of the visual field) can be quantified in two aspects: 1) the maximum distance over which interaction occurs (extent) and 2) the amount of loss in acuity (magnitude : Flom, 1991). The disruptive effect of simple surrounds, such as flanking bars, on target recognition is called 'contour interaction', and the effect of complex surrounds such as letters is called 'crowding' (Danilova & Bondarko, 2007).

In normal adult foveal vision, crowding only occurs over very small distances (3-5 arcmin: Levi, 2008; or 4-6 arcmin: Flom, 1991) at the resolution limit and the effect decreases if the target is slightly above the resolution limit (1 arcmin: Danilova & Bondarko, 2007; Flom, 1991). Other authors mention that crowding effects are absent in foveal vision, but yet already at 2° from the fovea the crowding effect already is quite pronounced (Levi, 2008). Foveal crowding thus is a controversial term when it is used in the context of adult normal vision (Strasburger, et al., 1991). However, extensive crowding effects do occur in the central visual field of strabismic amblyopes (Danilova & Bondarko, 2007; Strasburger, et al., 1991). Extensive foveal crowding has also been reported in other populations. From literature, we know that contour interaction and foveal crowding are developmental phenomena in individuals with NV and in individuals with abnormal visual input (for example due to central scotomas, visual deprivation during the critical period or fixational instability/nystagmus), but also in individuals with damage of the visual pathways, which is the case in periventricular leukomalacia (PVL: Jacobson, et al., 1996). In visually impaired (VI) children, it could be hypothesized that foveal crowding interferes with the ability to (learn to) read and reading rate and can thus have secondary effects on the acquisition of academic skills. Surprisingly, no interventions have been applied to reduce foveal crowding effects in VI children and adults.

This overview focuses on three groups that show excessive degrees of foveal crowding when compared to adults with NV: (1) children with NV, in this group foveal crowding is present until at least 11 years of age (Jeon, et al., 2010), (2) VI children and adults (Chung & Bedell, 1995; Pardhan, 1997; Pascal & Abadi, 1995), and (3) children with a cerebral visual impairment (CVI : Jacobson, et al., 1996; Pike, et al., 1994). In VI individuals, foveal crowding seems to persist much more and much longer than in individuals with NV (Pardhan, 1997). The diagnosis CVI is given when 1) there is vision loss in the absence of signs of anterior pathway disease, or 2) when

vision loss is greatly exceeding that which could be explained given the findings of ocular examination (Huo, Burden, Hoyt, & Good, 1999). We investigated whether Perceptual Learning (PL) is an effective training to reduce crowding effects. PL is based on the notion that practicing visual tasks can lead to dramatic and long-lasting improvements in performing these tasks (Huckauf & Nazir, 2007). This systematic review has a twofold goal: (1) comparing the amount of (foveal) crowding in the three groups of interest, and (2) investigating the potential of PL to reduce crowding effects.

## METHODS

### Systematic literature search

Studies were identified by searching electronic databases, scanning reference lists of full text articles that were assessed for eligibility and consultation with experts. The search was applied to PubMed, PsycINFO (Ovid) and Cochrane. The last search was run on 28 May 2012. No limitations regarding year of publication or language were applied. The search was developed by an experienced clinical librarian and the first author of the article. The following search terms were used to search for all databases: visual perception (MeSH term), contour interaction, crowding (MeSH term), crowded, and contour interactions. The search strategy in PubMed is presented in Table 3.1.

### Study selection

Titles and abstracts were assessed for eligibility by 2 reviewers (BH en FNB), using the inclusion criteria presented in Table 3.2. All stages of study selection, data extraction, and quality assessment were performed by two independent reviewers (BH en FNB). Disagreements during selection were solved by application of criteria, discussion and

**Table 3.1** *Search History in PubMed.*

Search	Most Recent Queries	Result
#10	Search #3 AND#9	409
#9	Search #4 OR #5 OR #6 OR #7 OR #8	8838
#8	Search contour interactions[tiab]	17
#7	Search crowded[tiab]	3090
#6	Search crowding[mesh]	1792
#5	Search crowding[tiab]	5095
#4	Search contour interaction[tiab]	40
#3	Search #1 OR #2	173402
#2	Search visual perception[tiab]	3310
#1	Search visual perception[mesh]	172470

**Table 3.2** *Inclusion criteria.*

<b>Population</b>	Children with Normal Vision up to 18 years Children and Adults with Visual Impairment Children with Cerebral Visual Impairment Adults with amblyopia (addressed for two intervention studies)
<b>Intervention</b>	Randomized controlled trials (n=0) Non-randomized intervention studies (n=4) Cohort studies (n=3) Case control studies (n=4) Cross sectional studies (n=11)
<b>Outcome measures</b>	Contour interaction area (n=7) Crowding ratio (n=8) Effects of Perceptual Learning on crowding (n=7)

consensus. Four articles presenting crowding ratios in children with amblyopia and children with NV were not included. These studies did not focus on our group(s) of interest.

### **Inclusion criteria**

Included quantitative studies focused on: 1) foveal crowding in children with NV up to 18 years, individuals with VI, and children with CVI up to 18 years, or 2) PL studies designed to reduce crowding effects, i.e. reducing contour interaction area or improving crowded acuity (foveal and peripheral). In order to increase data collection about interventions designed to reduce foveal crowding, we also included two intervention studies in adult populations with amblyopia. Studies which included individuals with diagnoses other than those specified above (e.g. dyslexia) were excluded. The term 'VI individuals' was used and no age limits were set for this group, because of the scarce amount of studies with regards to VI children.

### **Data extraction and quality assessment**

Quality of the included studies was evaluated independently by two reviewers (BH en FNB) using criteria for cross sectional and case-control studies (Higgins, 2011). Information for evaluation of the included studies was: number of participants, clear outcome definition, and results (reporting confidence intervals and thresholds in case they were presented).

## Statistical analysis

There were not enough studies using similar paradigms and studies provided too little information on quantitative outcomes to conduct a meta-analysis or sensitivity analysis. Due to methodological heterogeneity, the results of the studies are presented in a narrative way.

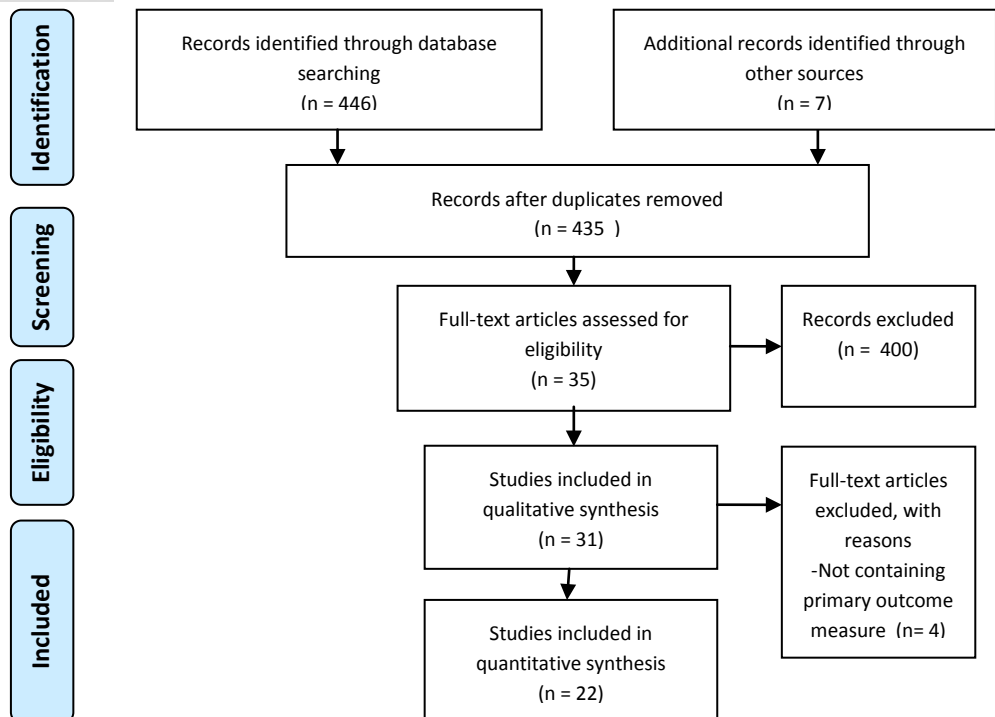
## RESULTS

### Results of search and selection process

The search of PubMed, PsycINFO (Ovid) and Cochrane databases provided a total of 446 citations. After adjusting for duplicates 435 remained. Seven articles were identified by experts the criteria (see Table 3.2). After full text inspection, another 4 articles were excluded because they did not contain our primary outcome measures. Of the included studies, 22 were quantitative studies, 8 additional studies were included to clarify the core concepts of (foveal) crowding and contour interaction (Balas, et al., 2009; Bouma, 1970; Hariharan, et al., 2005; Huo, et al., 1999; Strasburger, et al., 1991). See PRISMA flow chart Figure 3.1. Of the included quantitative studies, 4 were non-RCT's, 3 were cohort studies, 4 were case control studies and 11 were cross-sectional studies.



**Figure 3.1:** PRISMA 2009 Flow Diagram.



## Description of included studies

The review focuses on three specific outcome measures: (1) the contour interaction area, (2) the crowding ratio, and (3) effects of PL on crowding. Seven studies were found which measured the contour interaction in the groups of interest. Eight studies were found on crowding ratios. Seven studies were found which measured crowding as an outcome measure after a PL intervention. Table 3.3a presents the type of observational studies that were included, the characteristics of these studies and the outcome of the studies. Table 3.3b presents the characteristics of the intervention studies that were included.

### 1 Contour interaction area

Seven studies on the influence of flanking bars or -contours on object recognition (at the resolution threshold) were found. Five of these were conducted in a population of children with NV (Bondarko, 2005; Jeon, et al., 2010; Manny, Fern, & Loshin, 1987; Semenov, Chernova, & Bondarko, 2000) and two were conducted in a population of VI adults (Chung & Bedell, 1995; Pascal & Abadi, 1995). Often, the distances over which contour interaction occurs are expressed in steps of the Minimum Angle of Resolution (MAR). Five MAR is equal to the size of one optotype. The outcome of three studies on the full extent of the contour interaction area are presented in Figure 3.2 (Jeon, et al., 2010; Manny, et al., 1987; Semenov, Chernova, & Bondarko, 2000).

In three studies on contour interaction in children with NV the dependent measure was the full extent of the interaction area (the maximum distance over which interaction occurs) (Jeon, et al., 2010; Manny, et al., 1987; Semenov, Chernova, & Bondarko, 2000).

Two studies measured the distance at which contour interaction degraded target recognition most (Bondarko, 2005; Manny, et al., 1987) and one study measured contour interaction at 2.5 MAR (Fern, Manny, Davis, & Gibson, 1986). The full extent of the interaction area seemed to be approximately 7 MAR in children (or the size of 1 ½ optotype, inhibition zone size), which is 1.5-3× as large as the interaction area seen in adults) (Jeon, et al., 2010; Semenov, Chernova, & Bondarko, 2000). The maximum contour interaction area (distance at which object recognition is most degraded by surrounding contours) was approximately 2.5× MAR according to Bondarko et al. (2005) and 0.71×MAR in the study by Manny et al. (1987). The study by Fern et al. (1986) found no difference between contour interaction in children and adults when flankers were placed at 2.5×MAR. The three most recent studies showed a clear age effect (Bondarko, 2005; Jeon, et al., 2010; Semenov, Chernova, & Bondarko, 2000), with increased contour interaction until adolescence. Two studies found no age effect (Fern, et al., 1986; Manny, et al., 1987). It should be mentioned that the design of these studies differed with respect to response alternatives. Also, the

**Table 3.3a** *Type of study and outcome for observational studies.*

<b>Reference</b>	<b>Type of study</b>	<b>Number of participants, group (and age).</b>	<b>Method</b>	<b>Outcome</b>
<b>Fern 1986</b>	Cross-sectional	N=105 Children (2-7y) NV N=16 Adults NV	Stimulus: Isolated Landolt C/Landolt C with flanking bars at 3m. <u>Threshold symbol size:</u> 75% <u>Flanker spacing:</u> 2.5 MAR <u>Foveal/Eccentric:</u> foveal	Contour interaction area  Children showed the same contour interaction effects as adults at $2.5 \times$ MAR.
<b>Manny 1987</b>	Cross-sectional	N=13 Children (3-4y) NV N=5 Adults NV	Stimulus: Isolated Landolt C/Landolt C with flanking bars at 3m. <u>Threshold symbol size:</u> 90-95% <u>Flanker spacing:</u> 0-8.52 MAR <u>Foveal/Eccentric:</u> foveal	Contour interaction area (see Figure 3.2).
<b>Chung 1995</b>	Case-control	N=4 Adults CN N=6 Adults NV	Stimulus: Isolated Landolt C/Landolt C with flanking bars at 4.1m. <u>Threshold symbol size:</u> 50% <u>Flanker spacing:</u> 1, 2, 5, or 10 MAR <u>Foveal/eccentric:</u> foveal	Contour interaction area (see Figure 3.3).
<b>Pascal 1994</b>	Case-control	N=6 Adults NV N=6 Adults idiopathic CN N=6 Adults with albinism	Stimulus: Isolated Landolt C/Landolt C with flanking bars (3m or 6m). <u>Threshold optotype size:</u> 50% <u>Flanker spacing:</u> 1, 5 MAR <u>Foveal eccentric:</u> foveal	Contour interaction area (see Figure 3.3).

<p><b>Semenov 2000</b></p>	<p>Cross-sectional</p>	<p>N=140 Children (3-9y) NV  N=4 Adults NV</p>	<p><u>Stimulus:</u> Isolated Landolt C/Landolt C with flanking bars at 4.3m. <u>Threshold optotype size:</u> 75% <u>Flanker spacing:</u> 3.75-10 MAR <u>Foveal/eccentric:</u> foveal.</p>	<p>Contour interaction area (see Figure 3.2).</p>
<p><b>Bondarko 2005</b></p>	<p>Cross-sectional</p>	<p>N=292 Children (8-17y) NV</p>	<p><u>Stimulus:</u> Isolated Landolt C, E-letters, Gratings/ Landolt C with flanking bars, E-letters with E-letters, Gratings by Gratings at 4.3m. <u>Threshold optotype size:</u> 75% <u>Flanker spacing:</u> 0-7 MAR. <u>Foveal/eccentric:</u> foveal</p>	<p>Contour interaction.  The maximum inhibition separation significantly decreased from approximately 2 MAR to 1.5MAR from age 8 to age 17.</p>
<p><b>Jeon 2010</b></p>	<p>Cross-sectional</p>	<p>N=59 Children (5-, 8-, 11y) NV  N=19 Adults NV</p>	<p><u>Stimuli:</u> Single Sloan E/Sloan E with gratings at 4.2m. <u>Threshold optotype size:</u> 79.1% <u>Flanker spacing:</u> started at 20MAR (10 reversals) <u>Foveal/eccentric:</u> foveal</p>	<p>Contour interaction area (see Figure 3.3.2).</p>
<p><b>Atkinson 1985</b></p>	<p>Cross-sectional</p>	<p><u>Study 1:</u> N=14 Children NV(5;3-6;2y) N=9 Mothers  <u>Study 2:</u> N=13 Children (3;1-4;1y) N=8 Mothers</p>	<p><u>Stimulus:</u> Single Landolt C/Landolt C surrounded by Os and Cs at 1.5-8.3m. <u>Interoptotype spacing:</u> 50% (line/circular configuration) <u>Foveal/eccentric:</u> foveal</p>	<p>Crowding ratio (see Figure 3.4).</p>

<b>Atkinson 1988</b>	Cross-sectional	N=47 Children (3-4y) N=12 Adults NV  N=12 Children NV(5-7y)	Stimulus: Single Sheridan Gardener card /5-letter Sheridan Gardener card at 3m and 6m. <u>Interprototype spacing: 50%</u> <u>Foveal/eccentric: foveal</u>	Crowding ratio (see Figure 3.4).
<b>Kothe 1990</b>	Cross-sectional	N=90 Children NV(4-11y)	Stimulus: Isolated acuity/Regan Repeat Letter acuity/Snellen acuity at 6m. <u>Interprototype size: 100%</u> <u>Foveal/eccentric: foveal.</u>	Crowding ratio (see Figure 3.5).
<b>Jacobson 1996</b>	Cross-sectional	N=13 Children CVI (5-14y)	Stimulus: LH single /LH line at 3m. <u>Interprototype spacing=100%</u> <u>Foveal/eccentric=foveal</u>	Crowding ratio (see Figure 3.5).
<b>Pike 1994</b>	Cross-sectional	N=42 Children (2-9y)  CVI	Stimulus: Single Sheridan Gardener /7-letter Sheridan Gardener at 6m. <u>Interprototype spacing:50%</u> <u>Foveal/eccentric: foveal</u>	Crowding ratio (see Figure 3.4).
<b>Pardhan 1997</b>	Case-control	N=18 VI Adults (42-85y) N=25 Adults NV (42-85y)	Stimulus: Isolated visual /Regan Repeat Letter Chart, Snellen Line chart at 6m. <u>Interprototype spacing: 100%</u> <u>Foveal/eccentric: foveal</u>	Crowding ratio (see Figure 3.5).
<b>Norgett 2011</b>	Cross-sectional	N=103 Children (4-9y)  NV	Stimulus: Single: Kay Picture Single, Single Sheridan Gardiner. 50%: Log MAR crowded acuity, Kay Picture Crowded Log MAR 100%: Sonksson Log MAR at 6m.	Crowding ratio (see Figure 3.4 and 3.5)



		Interoptotype spacing: see above. Foveal/eccentric: foveal		Crowding ratio							
<b>Huerneman 2012</b>	Case-control	N=75 Children (4-8y)	NV NV		$C^{2.6}$	$C$ (LH) <sup>2.6</sup>	$C^{2.6}$ far (5m)	LH <sup>2.5</sup> %	LH <sup>50</sup> %	LH <sup>100</sup> %	
		Stimulus: C-test, LH-version C-test, LH line test with 25%, 50% and 100% spacing at 40cm. C-test at 5m.			NV	1.39	1.36	1.17	1.16	1.09	1.09
		Interoptotype spacing: see above. Foveal/eccentric: foveal			VI without CN	1.47	1.54	1.17	1.11	1.12	1.07
					VI with CN	1.78	1.78	1.51	1.24	1.22	1.13

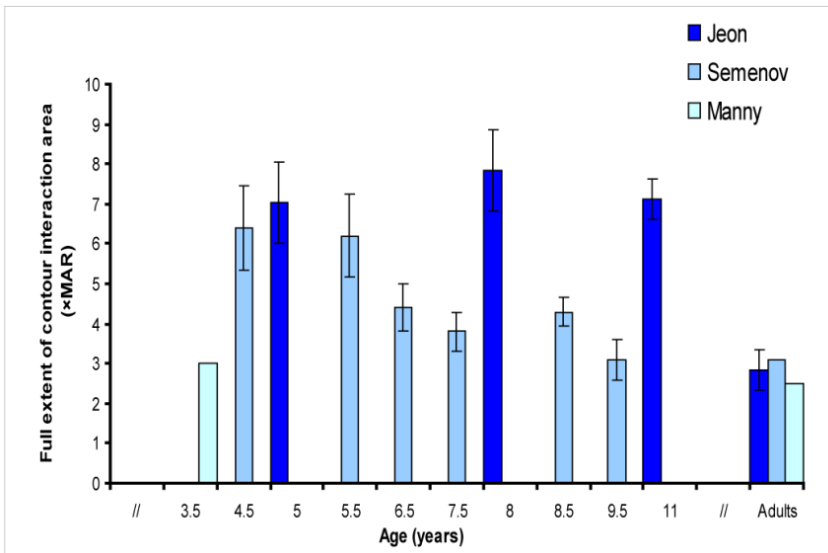
**Table 3.3b** *Type of study and outcome for intervention studies.*

Reference	Type of study	Number of participants, group	Method	Outcome
<b>Chung 2007</b>	Cohort study Perceptual Learning (PL)	N=8 Adults NV	<u>Training:</u> Identifying middle letter trigram at 10° in inferior visual field (0.8× x-height letter separation). 6 sessions=6000 trials (6 days) <u>Pre-test/Post-test</u> 1) reading speed for 6 print sizes; 2) flanked letters identification at 5 separations (0.8×,1×,1.25×,1.6×, and 2×).	1) Maximum reading speed did not improve significantly. Significant reduction in critical print size after training. 2) Accuracy for identifying target in a trigram improved significantly (88% improvement). Spatial extent decreased significantly from 1.12x to 0.69x the letter size after training.
<b>Green 2007</b>	Non-Randomised controlled trial (Non-RCT) Video-game playing (VGP)	Exp. Group: N=16 Adults NV Control Group N=16 Adults NV (all non-video game players)	<u>Training:</u> -Experimental group: high intensity action videogame; -Control group: less visually intense videogame. 30h training (4-6 weeks) <u>Pre-test/Post-test:</u> Identification middle T trigram at 0°, 10° and 25° (VGPs vs. non-VGPs).	Only the action videogame group showed a significant decrease in crowding region (all eccentricities). No improvement single T acuity after training.
<b>Huckauf 2007</b>	Non-RCT PL	<u>Training 1:</u> N=10 (no training); N=10 (training with feedback)	<u>Training 1:</u> Identify flanked target letters. Always same target/flank combination at 4° and 7°, 1° center-to-center spacing (25 min. training).	<u>Training 1:</u> Crowding significantly reduces for trained strings and less for untrained strings (specificity effect). No difference between training groups. <u>Training 2:</u> Crowding effects do not reduce when letter

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		<p>target); N=10 (training with feedback flanker).</p> <p><u>Training 2:</u> N=4</p> <p><u>Training 3:</u> N=24</p> <p><u>Training 4:</u> N=11 Adults NV</p>	<p><u>Training 2:</u> Random assignment trained flankers (letters and unfamiliar symbols). Eccentricities 1°, 4° and 7°. 2h/day (3 days; 1980 trials).</p> <p><u>Training 3:</u> String training at a defined eccentricity of 3° in one of the two visual fields. Participants were measured at three time points: after 144 trials (short training), and an additional 720 trials (long training). Twelve were retested 24h after training.</p> <p><u>Training 4:</u> Same as Experiment 3, but also presentation of isolated letters during training and test.</p>	<p>combinations differ from trial to trial (specificity effect).</p> <p><u>Training 3:</u> 16% improvement after short training and 28% improvement after long training. After 24h, performance was significantly better than at baseline, but did not differ from performance after short or long training.</p> <p><u>Training 4:</u> Transfer occurred earlier when words were used as stimuli. Isolated letter recognition showed no significant improvement after training, flanked letter recognition improved significantly.</p>
<b>Maniglia 2011</b>	Cohort study PL	N=8 Adults NV	<p><u>Training:</u> Contrast detection of a Gabor target presented in at 4° in the presence of co-oriented and co-aligned high contrast Gabors. 160 sessions≈60,000 trials (8 weeks)</p> <p><u>Pre-test/Post-test</u> 1) Visual Acuity 2) Crowded acuity 3) Contrast sensitivity</p>	<p>1) Visual Acuity did not improve in peripheral vision. 2) Crowding reduced significantly in peripheral vision. Observers could better identify a target in a cluttered background. 3) Training lateral interactions only reduced contrast sensitivity at the highest spatial frequency used.</p>
<b>Li 201</b>	Non-RCT VGP	N=10 (action videogame group) N=3 (non action	<p><u>Training:</u> Action videogame group (n=10), non-action videogame group (n=3) and cross-over control group (n=7). 40-80h videogame playing.</p>	<p>1.1) On average 1.4 to 1.6 lines improvement of acuity after action videogame; 1.2) Non-action videogame players improved 1.5 lines on crowded letters and 0.8 lines for single letters. Patching group no improvement in visual acuity after 20h.</p>

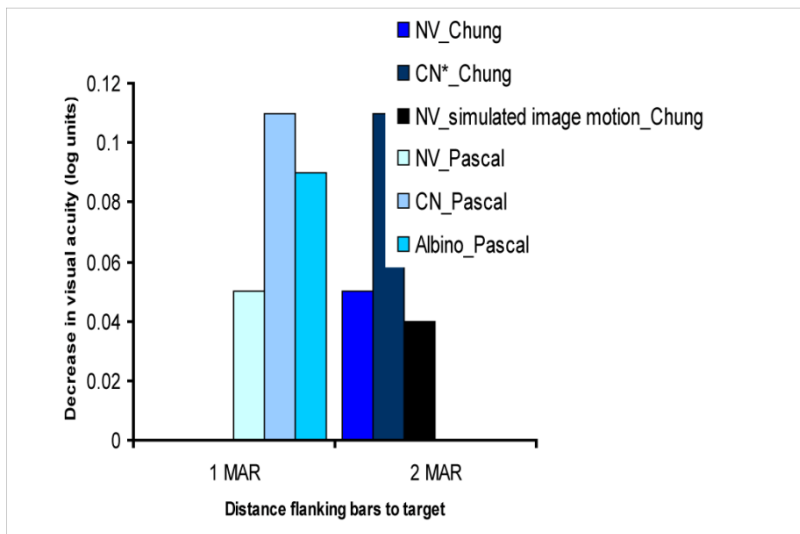
		videogame group) N=7 (crossover control group; 20h occlusion, 40h videogame therapy)  Adults with amblyopia	<u>Pre-test/Post-test</u> 1) Visual Acuity (Bailey-Lovie logMAR charts) 2) Positional acuity; 3) Spatial attention; 4) Stereopsis.	Recovery crowded acuity slightly faster than single. Mean crowding index did not significantly improve. 2) Positional acuity improved significantly; 3) Spatial attention improved significantly; 4) Stereopsis improved significantly.
<b>Sun 2011</b>	Cohort study  PL	N=6 Adults NV	<u>Training:</u> Same as Chung (2007).  <u>Pre-test/Post-test</u> Identification letter in 2 flanking conditions (unflanked/flanked) crossed with four noise levels.	Accuracy improvement in identifying letters in flanked condition without noise (22%). Training improves efficiency or equivalent input noise in a subject-dependent matter.  -Retained improvements after 1-6 months.
<b>Hussain 2012</b>	Non-RCT  PL	N=10 (of which 5 served as a control group that trained after performing 2 pre-tests). Adults with amblyopia  N=10 (training group) N=7 (control group) Adults NV	<u>Training:</u> Identifying central target letter (1.4×threshold size) surrounded by 4 letters in each cardinal orientation. Adults with amblyopia=foveal training. Adults with NV=4° eccentricity. 8-14 sessions (3600-9600 trials)  <u>Pre-test/Post-test</u> 1) unflanked acuity fellow eye; (2) unflanked acuity amblyopic eye; (3) flanked acuity fellow eye at a spacing of 1.1× letter size; (4) flanked acuities amblyopic eye at spacing of 1.1×, 1.2×, and 1.4× letter size.	1) Unflanked and flanked acuity both significantly improved in the fellow eye. Difference not significant. 2) Unflanked acuity improved significantly. 3) More progress for flanked than unflanked acuity. Significant improvements on Bailey-Lovie chart on average 1.5 lines. Comparable results for adults with NV in periphery (no improvement for control group).  Two follow up participants performed additional sessions and showed a further significant decrease in their crowding ratio's (after performing 1-11 additional sessions).



**Figure 3.2** Full extent of the contour interaction area. Figure 3.3.2 presents the results of three studies that have measured the full contour interaction area in children and adults with NV. Differences between the studies can partially be explained by the different optotypes used. The study by Semenov used Landolt C's with flanking bars and the study by Jeon et al. used E-gratings surrounded by gratings. E-gratings are more difficult to identify than C-rings for children, which might explain the larger contour interaction areas when E-gratings are used. Error bars  $\pm 1$  s.e.m.

three most recent studies (Bondarko, 2005; Jeon, et al., 2010; Semenov, Chernova, & Bondarko, 2000) were more sensitive at measuring differences than the earlier studies (Fern, et al., 1986; Manny, et al., 1987), because results were based on more trials, had a larger age range, were analysed per year group and step sizes were smaller. Studies on contour interaction show that the full extent of the contour interaction area is 1.5-3 $\times$  as large in children with NV as in adults with NV.

There were two studies on contour interaction in VI adults (Chung & Bedell, 1995; Pascal & Abadi, 1995; see Figure 3.3). One study compared the full contour interaction area, the point of maximum contour interaction, and the peak magnitude of contour interaction between adults with NV and adults with congenital nystagmus (CN) (Chung & Bedell, 1995). Another study focused on the area at which contours caused maximum interaction effects and compared between three subject groups: adults with NV, adults with albinism and adults with CN (Pascal & Abadi, 1995). Both studies found an increased amount of contour interaction in adults with CN when compared to controls. Adults with albinism did not differ from adults with NV. Adults with CN experience more contour interaction (interaction area is

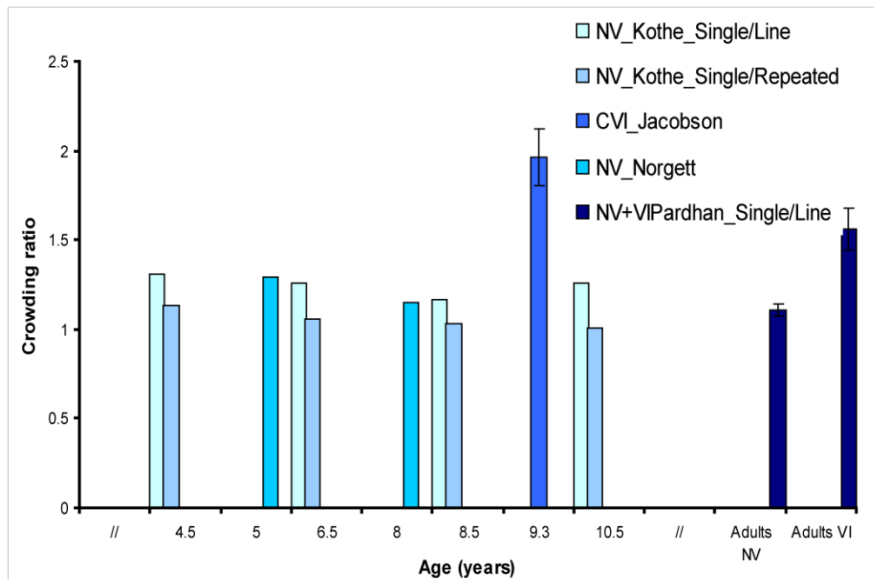


**Figure 3.3** The magnitude of contour interaction effects at 1 and 2 MAR. Figure 3.3 presents the results of two studies which have measured the magnitude of the contour interaction effect in adults with normal vision, adults with congenital nystagmus (CN) and adults with albinism. As can be seen, the magnitude of the effect (defined by the decrease of visual acuity in log units) is the largest in adults with CN in both studies. Standard errors of the mean were not provided.

approximately twice as large as in adults with NV). The magnitude of contour interaction in terms of degradation of resolution acuity was also larger in adults with CN (1/2 line in adults with NV and 1.1 line in adults with CN). In the presence of a black background, degradation of resolution acuity was even larger (1.4 line for adults with NV and 2.4 lines for adults with CN). Fixational instability was simulated in adults with NV in a second part of the study (Chung & Bedell, 1995). This degraded performance, but did not explain the effect of the contour interaction in individuals with idiopathic CN. The authors mention the possibility of a sensory amblyopia effect as a consequence of the incessant image motion coupled with sizeable astigmatic refractive errors during the period of visual plasticity in early life. Duration of the foveation period, contrast, background colour and orientation played an important role in predicting the amount of contour interaction in the CN group.

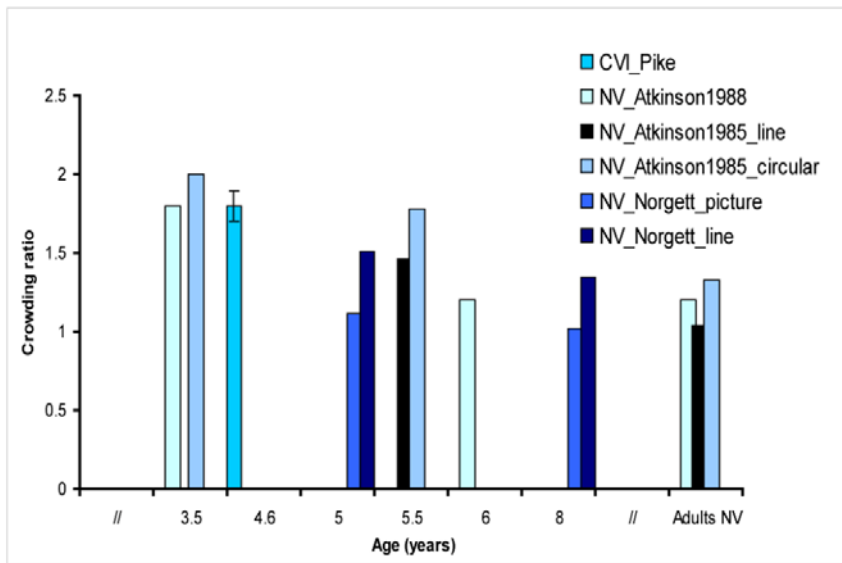
## 2 Crowding ratio

Crowding ratios can be calculated by dividing the single decimal line acuity by decimal acuity when optotypes are surrounded. This can be seen as a method to measure the magnitude of the crowding effect. Eight studies were found which measured single and line acuity and crowding ratios were presented or could be calculated from the



**Figure 3.4** Crowding ratios measured with charts with 100% interoptotype spacing. Figure 3.4 presents the results of four studies which measured crowding ratios in different populations: children and adults with normal vision (NV), children with cerebral visual impairment (CVI), and visually impaired (VI) adults. Children with CVI and adults with VI showed higher crowding ratios than respectively children with NV and adults with NV. Error bars  $\pm 1$  s.e.m.

data presented in the study. As mentioned earlier, due to methodological heterogeneity we could not perform a meta-analysis. However, there were studies using somewhat identical methods. Four comparable studies with interoptotype spacing of 100% are presented in Figure 3.4 (Jacobson, et al., 1996; Kothe & Regan, 1990a; Norgett & Siderov, 2011; Pardhan, 1997) and four studies with interoptotype spacing of 50% are presented in Figure 3.5 (Atkinson, Anker, Evans, Hall, & Pimm-Smith, 1988; Atkinson, Pimm-Smith, Evans, Hradings, & Braddick, 1985; Norgett & Siderov, 2011; Pike, et al., 1994). Five of these studies were conducted in a population of children with NV (Atkinson, et al., 1988; Atkinson et al., 1985; Huurneman, Boonstra, Cillessen, et al., 2012; Kothe & Regan, 1990a; Norgett & Siderov, 2011). One of these studies compared crowding ratios found in children with NV, VI children without CN and VI children with CN. The study found significantly higher crowding ratios in VI children with CN than in VI children without CN and children with NV (Huurneman, Boonstra, Cillessen, et al., 2012). This is the only study we found that measured the crowding ratio for near vision (40 cm) and distance vision (5 m). All other studies only measured crowding for distance vision (1.5-6 m). Another exception is that this study used charts with proportional and charts with absolute interoptotype spacing. The charts with absolute spacing were most sensitive



**Figure 3.5** Crowding ratios measured with charts with 50% interoptotype spacing. Figure 3.5 presents the results of four studies which have measured crowding ratios in children and adults with normal vision (NV) and children with cerebral visual impairment (CVI). Line means that the crowding ratio was calculated by dividing the single through the line acuity score and circular means that the crowding ratio was calculated by dividing the single acuity through the acuity score that was measured when a target symbol was surrounded by 6 symbols surrounding the target in all directions. A clear age related reduction of the crowding ratio in is observed in children with NV. Error bars  $\pm 1$  s.e.m.

to pick up crowding effects (Huurneman, Boonstra, Cillessen, et al., 2012). Another study compared performance on a Repeat letter chart, a Line letterchart and a single letter chart, to investigate whether crowding effects were due to gaze control/selection defects (in which case the Repeat letter chart would show better acuity values than Line acuity charts) or lateral interaction effects (in which case Line chart scores are equal to or better than Repeat chart scores) in children with NV (Kothe & Regan, 1990a). Children showed higher scores on Repeat letter charts than on Snellen charts and the authors concluded that gaze-selection or gaze-control could be seen as a contributing factor of lower scores on the Snellen chart.

Letter optotypes evoked more crowding than symbols and smaller interoptotype separation resulted in poorer acuity scores (50% vs. 100% interoptotype separation : Norgett & Siderov, 2011). The magnitude of the crowding effect, e.g. the influence of crowding on acuity, shows that children with NV score 1-2 lines lower on the visual acuity chart when interoptotype separation is 50% compared to single optotype acuity (depending on age) and the amount of crowding becomes even larger in a circular



configuration of target and flankers (Atkinson, et al., 1988; Atkinson et al., 1985). The large crowding effect at 50% interoptotype separation is in agreement with the studies on contour interaction described above which found maximum interaction effects when bars were placed at 2-2.5 $\times$  MAR (Jeon, et al., 2010; Semenov, Chernova, & Bondarko, 2000). Two studies did not provide the crowding ratio, but presented isolated and line scores, so crowding ratios could be calculated (Kothe & Regan, 1990a; Norgett & Siderov, 2011). Two other studies did not present standard deviations or standard errors (Atkinson et al., 1988; Atkinson et al., 1985). None of these studies presented cut-off scores to indicate extreme crowding, but used group statistics to determine differences (Atkinson et al., 1988; Atkinson et al., 1985; Huurneman et al., 2012; Kothe & Regan, 1990; Norgett & Siderov, 2011).

One study compared the crowding ratios of VI adults with those found in age-matched adults with NV (Pardhan, 1997). This study compared Repeat Letter acuity with a Line acuity and Single Letter acuity task. In total 83% of VI adults showed visual crowding (defined here as crowding ratio  $>1$ ). Thirty-nine per cent showed gaze-selection problems and 56% showed lateral interaction effects (see Figure 3.5 for Single/line ratios). The enhanced crowding effects in this particular population might be due to the use of peripheral fixation, where contour interaction effects are larger. Rehabilitation implications are that if contour interactions are the main cause for a decrease in reading ability, efforts should be directed at designing reading material in such a way that contour interaction effects are minimized. For patients with gaze selection deficits, therapies to improve accurate gaze selection would be beneficial (Pardhan, 1997).

Two studies have investigated crowding ratios in children with CVI (Jacobson, et al., 1996; Pike, et al., 1994). Both studies found enhanced crowding effects in this population. One study (Pike, et al., 1994) investigated patterns of visual impairment in children ( $n=42$ ) with different lesions seen on ultrasound before 35 weeks gestational age (severe leukomalacia, large intra ventricular haemorrhages (IVH), or cerebral infarction). Excessive crowding, here defined as a ratio  $\geq 2$ , occurred in 13 out of 29 children and especially in those with impaired acuity ( $\leq 0.30$  or  $\leq 6/18$ ) Furthermore, the authors found that visual impairments are more common in association with ischemic lesions (leukomalacia and infarcts) than in association with haemorrhagic lesions, but abnormal crowding ratios were not associated with any particular lesion location on MRI. In contrast, the pattern of visual impairment associated with PVL entails more specific and extensive visual dysfunction (Jacobson, et al., 1996). Line acuity for near vision could be tested in 9 of 13 children. A crowding ratio for distance vision could be calculated for 10 children. The crowding ratio was significantly elevated in this group (see Figure 3.4). Reading was difficult and although the children were able to read short words, they were unable to continue on if the text contained

long words on a line. They had difficulties maintaining track, and retracing when they left off. The authors point out that crowding is considered to be one of the major obstacles in fluent reading in children with PVL. Ophthalmological findings report horizontal nystagmus in 12 of 13 children and problems with saccades and pursuit movements.

In sum, it can be concluded that crowding is present in children with NV till adolescent age. The magnitude of the crowding effect, e.g. the influence of crowding on acuity, shows that children with NV score 1-2 lines lower on the visual acuity chart when interoptotype separation is 50% compared to single optotype acuity (depending on age) and the amount of crowding increases in a circular configuration of target and flankers. There seems to be agreement that the following factors are predictive for the extent of crowding in children with NV: gaze selection or gaze control, configuration (circular configuration of stimuli evokes more crowding than linear configuration), maturation of visual areas beyond V1 and cognitive development. In VI adults, acuity is 2 lines lower when optotype separation is 100% compared to single optotype acuity (it was approximately half a line in adults with NV). The effects are due to use of peripheral fixation, gaze selection deficits and lateral interaction effects. In children with CVI, crowding ratios were elevated in both studies (2-3 lines lower score on line acuity chart compared to single acuity with 100% optotype spacing). Specific predictors of the amount of foveal crowding in children with CVI are: kind of lesion (ischemic lesion is associated with poorer visual outcome than hemorrhagic lesions), oculomotor deficits (inability to fixate), presence of nystagmus, and low acuity ( $\leq 0.30$  or  $\leq 6/18$ ).

### **3 Effects of Perceptual Learning on crowding**

Seven articles were specifically about reducing crowding with the help of PL techniques or videogame playing (Chung, 2007; Green & Bavelier, 2007; Huckauf & Nazir, 2007; Hussain, Webb, et al., 2012; Li, et al., 2011; Maniglia et al., 2011; Sun, et al., 2010). Five of these studies evaluated the influence of PL on the reduction of crowding effects (Chung, 2007; Huckauf & Nazir, 2007; Hussain, Webb, et al., 2012; Maniglia, et al., 2011; Sun, et al., 2010). Four studies were conducted in a population of adults with NV (Chung, 2007; Huckauf & Nazir, 2007; Maniglia, et al., 2011; Sun, et al., 2010), and one compared the influence of PL on crowding in adults with amblyopia and adults with NV (Hussain, Webb, et al., 2012). We found two studies on videogame playing and the reduction of crowding (Green & Bavelier, 2007; R. W. Li, et al., 2011). One was conducted in a population of adults with NV (Green & Bavelier, 2007) and one was conducted in a population of adults with amblyopia (Li, et al., 2011).

A non-Randomized Controlled Trial (non-RCT) investigated the effect of PL on the reduction of crowding (Huckauf & Nazir, 2007). In the PL study (Huckauf & Nazir, 2007), the training period in this study was very short (25 minutes), the groups were relatively small (N=10) and the authors did not measure effects of PL on improvements on acuity measures. However, there was improvement on flanked letter recognition. A specific learning effect for trained strings was found. A second non-RCT showed that foveal crowding ratios and visual acuity in adults with amblyopia and peripheral crowding ratios in adults with NV improved significantly after 8-14 sessions of PL (1.5 lines on average) (Hussain, Webb, et al., 2012). Three cohort studies on PL and the reduction of crowding effects in the periphery showed that, in adults with NV, accuracy for identifying flanked letters improved significantly (Chung, 2007; Maniglia, et al., 2011; Sun, et al., 2010), and isolated letter acuity did not improve (Maniglia, et al., 2011), and the reduction in crowding effects was retained up to at least 6 months (Chung, 2007; Sun, et al., 2010). Again, sample sizes were very small in this study (N=6-8). Thus, there are indications that PL reduces crowding effects, but it also has the potential to improve flanked and unflanked acuity after training on a crowded letter identification task in amblyopic foveal and normal peripheral vision (Hussain, Webb, et al., 2012).

A non-RCT was conducted in a population of adults with NV and evaluated whether (action) videogame playing (VGP) has the potential to reduce crowding effects in central and peripheral vision (Green & Bavelier, 2007). This study found that crowding effects decreased significantly after action VGP, but crowding effects did not decrease in the control group which trained with a less visually-intense non action videogame. However, the number of participants was relatively small (N=16), and the effect size of the reduction of the spatial extent of crowding was rather small ( $\eta_p^2 = .14$ ). Isolated acuity did not improve after VGP. A second non-RCT study, with a more extensive training period conducted in a population of adults with amblyopia, showed significant improvement in flanked and unflanked visual acuity after 40-80h of (action) videogame playing (on average 1.5 letter lines : Li, et al., 2011). There was no difference in the amount of improvement in flanked and unflanked acuity. The mean crowding index did not improve significantly after videogame playing (Li, et al., 2011), as was seen in the PL study in adults with amblyopia (Hussain, Webb, et al., 2012). The improvement in visual acuity was found for action videogames and non-action videogames. Although this study showed impressive recovery in visual acuity that is about 5-fold faster than that expected after occlusion therapy, the authors also point out that the study contains several limitations: small sample size, lack of randomization, and differences in number of groups. The conclusion is that a large-scale randomized study is needed to confirm the therapeutic value of videogame treatment in clinical situations.

There is stronger evidence for PL as an effective method to specifically reduce crowding effects than VGP. Although it has never been studied, it is plausible that PL could improve visual functioning in children with a (cerebral) visual impairment, because the factors that seem account for foveal crowding in this group are: fixational instability, gaze selection problems, poor contrast sensitivity, poor visual acuity, large interaction areas (possibly due to amblyopia effects) and short foveation periods. The above studies illustrated the prospects of PL on: reducing critical spacing (or contour interaction areas) or improvement of recognition for crowded stimuli (Chung, 2007; Green & Bavelier, 2007; Huckauf & Nazir, 2007; Hussain, Webb, et al., 2012; Li, et al., 2011; Maniglia, et al., 2011; Sun, et al., 2010), improvement on clinical measures of visual acuity (Hussain, Webb, et al., 2012; Li, et al., 2011), improving contrast sensitivity (Maniglia, et al., 2011), improving ocular alignment and training non retinotopic higher brain processes engaged in attention and decision making (Li, et al., 2011).

## **DISCUSSION**

The goal of the present review was to compare studies which measured foveal crowding in three specific groups and explore possible interventions for crowding in children with a (cerebral) visual impairment. An important and striking conclusion must be that no interventions have been evaluated in our groups of interest, despite the abnormal crowding ratios in children with a (cerebral) visual impairment (Huurneman, Boonstra, Cillessen, et al., 2012; Jacobson, et al., 1996; Pike, et al., 1994). It is also surprising that there are so few quantitative studies which have measured crowding in the VI child population and studies use different cut-off points to determine what quantifies abnormal crowding. The first goal of this overview was to describe the manifestation of the crowding phenomenon in children with NV (1), the VI group (2) and children with CVI (3), because it is conceivable that different factors and mechanisms are involved in these groups. However, different paradigms were used to measure crowding (methodological heterogeneity) and therefore results were presented in a narrative way. Factors that were identified to influence crowding in children with NV are: development of gaze selection/control (Huurneman, Boonstra, Cillessen, et al., 2012), configuration of the stimulus (Atkinson et al., 1985), cognitive development (Atkinson et al., 1985; 1988), and maturation of cortical structures beyond VI that are involved in the integration of local information (Jeon, et al., 2010). Factors influencing crowding in the VI group were: fixational stability (Chung & Bedell, 1995; Pascal & Abadi, 1995), background color (Chung & Bedell, 1995), contrast (Pascal & Abadi, 1995), orientation (Pascal & Abadi, 1995), and the presence of central scotomas (Pardhan, 1997). In the VI group, there is consistent evidence that individuals with CN experience contour interaction over larger interaction areas and

performance is more degraded by nearby contours in this group than in a control group with NV (Chung & Bedell, 1995). There is one study which shows that adults with a visual impairment show elevated crowding ratios, this study mentions that these results could be due to eccentric fixation in this group (Pardhan, 1997). There is one study which measured crowding in VI children, and this study found significantly higher crowding ratios for VI children with nystagmus than VI children without nystagmus and children with NV (Huurneman, Boonstra, Cillessen, et al., 2012). When interoptotype spacing is small, children with NV show a smaller loss of acuity than VI children. It might be reasoned that children with a congenital visual impairment may have developed amblyopia as a secondary symptom to their altered visual development (Chung & Bedell, 1995; Pascal & Abadi, 1995). Findings in the CN group suggest that this group could directly benefit from reduced contrast, a white background and proportionally larger interoptotype spacing (Chung & Bedell, 1995). Only one study could be found on crowding in the presence of albinism and this study provided no evidence of increased crowding compared to controls (Pascal & Abadi, 1995). Children with CVI, especially those with PVL, experienced abnormal crowding effects which can be related to the degree and kind of cortical trauma (ischemic lesions and infarcts seem to be more predictive of abnormal visual function than hemorrhages) and ability to fixate (Jacobson, et al., 1996; Pike, et al., 1994). This is a consistent finding in the studies that were included for this overview. Visual functioning in children with CVI is affected in different areas: visual fields are constricted (due to damage in the optic radiation), the majority of children exhibit nystagmus or strabismus, subnormal visual acuity, excessive crowding, and problems in simultaneous perception (Jacobson, et al., 1996; Pike, et al., 1994).

The last section was about interventions that have been designed to reduce crowding. Seven studies were found that specifically aimed at reducing crowding (Chung, 2007; Green & Bavelier, 2007; Huckauf & Nazir, 2007; Hussain, Webb, et al., 2012; Li, et al., 2011; Maniglia, et al., 2011; Sun, et al., 2010). The intervention studies that were found have a small sample size, and we found no interventions for our groups of interest. The interventions discussed above therefore should be seen as pilot studies. The small sample size and the differences in group numbers might bias the outcome and this review emphasizes the need for large randomized controlled studies. However, the studies that we did find showed that the PL techniques were more effective in specifically reducing crowding effects than the videogame playing studies. Three studies demonstrated that foveal resolution in adults with NV and adults with amblyopia can be enhanced by training (Green & Bavelier, 2007; Hussain, Webb, et al., 2012; Li, et al., 2011). The technique could be applied to reduce foveal crowding effects in individuals with congenital nystagmus, central scotomas, and children with CVI. Crowding effects, or inappropriately large integration areas, in the normal

periphery and foveal amblyopic vision have been explained by extended pooling at a stage following the stage of feature detection (Balas, et al., 2009; Hariharan, et al., 2005). This review illustrates that there is accumulating evidence that the normal periphery and foveal amblyopic vision can be fine-tuned by excessive presentation of challenging (crowded) stimuli. Because of sensory amblyopia effects (Pascal & Abadi, 1995) and fixational instability in our groups of interest (Huurneman, Boonstra, Cillessen, et al., 2012; Jacobson, et al., 1996; Pardhan, 1997; Pike, et al., 1994), PL could also work for children with a (cerebral) visual impairment. This review illustrates that there is a need for RCT's to investigate the value of PL in populations that experience excessive crowding effects (VI individuals with secondary amblyopia effect or nystagmus, children with CVI).

Thus, foveal crowding seems to be associated with an underdeveloped and/or understimulated visual system and practicing those areas of impairment can possibly produce improvements. Higher and lower level visual functions are interdependent and work together. Weaker lower level functioning in VI individuals, may lead to higher level impairments like the secondary amblyopia effect (Chung & Bedell, 1995; Pascal & Abadi, 1995). We have seen that gaze control and fixational stability play an important role in the amount of crowding in children with nystagmus and children with CVI, This fixational instability does not tell us the whole story. Research has delivered evidence that more contour interaction is present when contrast is stronger (Chung & Bedell, 1995). Whether foveal crowding can be reduced by practicing challenging tasks (such as letter identification in a busy visual field) and improving oculomotor control (through special designed games) is an interesting and novel question. PL literature on crowding stresses the importance of looking at individual capacities and when there are specific areas of impairment, these are the areas that the training should focus on.

## **CONCLUSIONS**

This overview shows that there is still much to learn about foveal crowding in children with a (cerebral) visual impairment and it is hard to compare findings because paradigms are different in nature. There seem to be differential mechanisms at play in the different subtypes of visual impairments. Evidence was found for enhanced crowding effects in individuals with CN, VI adults with central scotomas and children with CVI. Although literature was scarce, children with CVI showed the highest crowding ratios. Oculomotor control seems to play a crucial factor in predicting the amount of crowding. Interventions should be designed with these mechanisms kept in mind. Although there is a lack of large-scale randomized controlled trials on PL in patient populations, the findings presented in this review indicate that Perceptual

Learning is an effective technique to reduce peripheral crowding in adults with NV and foveal crowding in adults with amblyopia.

### **ACKNOWLEDGEMENTS**

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### **COMPETING INTERESTS**

No conflicting relationship exists for any author.

### **AUTHOR'S CONTRIBUTIONS**

Literature screening and selection was performed by BH and FNB. Data extraction and synthesis was performed by BH and FNB. Preparation of the first draft of the manuscript was done by BH and review and approval of the manuscript was performed by NB, AC, GR and RC. All authors read and approved the final manuscript.

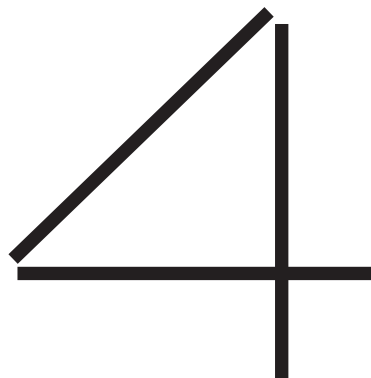
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Crowded task performance  
in visually  
impaired children:  
Magnifier versus large  
print

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**ABSTRACT**

**BACKGROUND:** This study compares the influence of two different types of magnification (magnifier versus large print) on crowded near vision task performance.

**METHODS:** Fifty-eight visually impaired children aged 4-8 years participated.

Participants were divided in two groups, matched on age and near visual acuity (NVA): [1] the magnifier group (4-6 year olds [n=13] and 7-8 year olds [n=19]), and [2] the large print group (4-6 year olds [n=12] and 7-8 year olds [n=14]). At baseline, single and crowded Landolt C acuity were measured at 40cm without magnification. Crowded near vision was measured again with magnification. A 90mm diameter dome magnifier was chosen to avoid measuring the confounding effect of navigational skills. The magnifier provided 1.7× magnification and the large print provided 1.8× magnification. Performance measures: [1] NVA without magnification at 40cm, [2] near vision with magnification, and [3] response time. Working distance was monitored.

**RESULTS:** There was no difference in performance between the two types of magnification for the 4-6 year olds and the 7-8 year olds ( $p$ 's = .291 and .246, respectively). Average NVA in the 4-6 year old group was 0.95 LogMAR without and 0.42 LogMAR with magnification ( $p < .001$ ). Average NVA in the 7-8 year was 0.71 LogMAR without and 0.01 LogMAR with magnification ( $p < .001$ ). Stronger crowding effects predicted larger improvements of near vision with magnification ( $p = .021$ ).

**CONCLUSIONS:** A magnifier is equally effective as large print in improving the performance of young children with a range of visual acuities on a crowded near vision task. Visually impaired children with stronger crowding effects showed larger improvements when working with magnification.

## INTRODUCTION

### **Magnifier use in visually impaired children**

Two methods can be used to enable VI children to access printed material: a magnifier or large print. Introducing a magnifier to a visually impaired (VI) child holds several benefits (Cox et al., 2009; Schurink, Cox, Cillessen, van Rens, & Boonstra, 2011). VI children show improved fine motor functioning and discover compensatory strategies (e.g., increase of ocular torticollis in case of nystagmus in order to utilize the neutral zone to acquire optimal fixation) after a magnifier training of six weeks (Reimer, Cox, Nijhuis-Van der Sanden, & Boonstra, 2011). Practical advantages of a magnifier over large print are that magnifiers enable children to inspect any written information at normal print size and they are less expensive than producing large print books (Alabdulkader, 2010). One study compared the influence of these two methods on the reading performance of VI students after a year of using them (Farmer, 2007). Reading performance improved more for the magnifier group ( $n=9$ ) than for the large print group ( $n=7$ ). However, weaknesses of this study were: a small sample size, no investigation of age effects, and no information on the amount of magnification. The current study takes these issues in account.

There are three reasons why differences in performance between the two methods might be expected in children. First, a magnifier might form an obstruction between the material of interest and the child. This will depend largely on the experience the child has with using a magnifier. Enlarged material has essentially the same general properties as the original version, and should therefore be less obstructive. Second, the image produced by a magnifier is deformed by optical aberrations such as axial and lateral colour, distortion, astigmatism and field curvature (Cakmakci & Rolland, 2007; Katz & Zikos, 1994). Because of these image distortions, a child has to attend more closely to the centre of the material and ignore the jumbled patterns and slight differences in appearance near the edge of the central area of magnification. The size of these effects is determined by the quality of the magnifier and the size of its field-of-view. Third, small (lateral) movements of the eyes or the head are augmented by the magnifier lens which can result in a less stable image when looking at the stimulus than when looking at large print. Although these effects may be small when considered in isolation, for young children they might nevertheless cause performance differences between both methods.

### **Crowding and magnification**

Visual crowding, defined as a poorer line acuity compared to single letter acuity, is more present in children with strabismus (Rydberg, et al., 1999), VI adults and VI children (Huurneman, Boonstra, Cillessen, et al., 2012; for a review, see Huurneman,

Boonstra, Cox, Cillessen, & van Rens, 2012). Crowding in foveal vision can be regarded as a normal developmental phenomenon (Jeon, et al., 2010). Therefore reading material for children consists of larger letters than would be predicted based on the single letter acuity. Crowding effects during early childhood could hinder the acquisition of reading skills (Jeon, et al., 2010), and could be a major obstacle to fluent reading (Jacobson, et al., 1996). Participants with normal vision do not benefit from increased letter spacing during reading (Tinker, 1963). Explanations for this finding are: disruption of word shape due to increased spacing and visual span as a limiting factor for response time (Legge, Mansfield, & Chung, 2001). In this study, single and line (crowded) acuity are measured with the Landolt C-test (Haase, 1993; Hohmann & Haase, 1982). Up to the age of 10-12 years a physiological crowding effect up to 2.5 log steps of acuity should be taken into account (Haase, 1993). VI children show a lag in reading skills and make more substitution errors than normally sighted peers (Douglas, Grimley, McLinden, & Watson, 2004; Douglas, Grimly, Hill, Long, & Tobin, 2002). Substitution errors occur when words are guessed because of poor orthographic pattern visibility. Crowding in foveal vision reduces the visibility of optotypes near the acuity threshold (Huurneman, Boonstra, Cox, et al., 2012). By magnifying the optotype, visibility improves.

This study compares the improvement in near vision with magnification and response time between a group of children working with a magnifier and a group of children working with large print. It was hypothesized that children would perform equally well with both methods if the confounding effect of navigational skills are of no influence. Children with larger discrepancies between single and crowded acuity were expected to show larger improvements with magnification (obtained by magnifier/large print and relative distance magnification [RDM] : Bevan et al., 2000). Magnification of a crowded optotype chart with fixed spacing will effectively increase absolute interoptotype spacing and thereby may remove the constraints of small interoptotype spacing for those children experiencing stronger crowding effects (Haase, 1993; Hohmann & Haase, 1982; Huurneman, Boonstra, Cillessen, et al., 2012).

## **MATERIALS AND METHODS**

### **Participants**

Participants were 58 VI children. Inclusion criteria in the sample were: age between 4 and 8 years, normal developmental level, birth at term ( $\geq 36$  weeks of gestation and normal birth weight), and a distance VA between 1.30 LogMAR (20/400)  $\geq 0.40$  LogMAR (20/50). Exclusion criteria were the presence of multiple impairments, intellectual disability, and central scotomas. Children were included from client databases of all Dutch vision rehabilitation centres. Table 4.1 presents the age and the crowded and single LogMAR near visual acuity (NVA) of both groups.

**Table 4.1** Characteristics of the two experimental groups (*M*, (*SD*)).

Age (yrs)	4		5		6		7		8	
Condition	M <sup>1</sup>	E <sup>2</sup>	M	E	M	E	M	E	M	E
N	4	4	5	8	4	7	6	7	6	7
Age months	54.3 (1.5)	52.5 (0.6)	66.6 (3.9)	67.5 (4.3)	76.3 (4.2)	78.9 (3.8)	88.7 (2.7)	88.6 (3.6)	99.7 (2.6)	99.6 (7.0)
NVA crowded <sup>3</sup>	1.05 (0.21)	1.13 (0.24)	0.98 (0.26)	0.86 (0.22)	0.90 (0.19)	0.87 (0.33)	0.62 (0.16)	0.63 (0.16)	0.85 (0.12)	0.74 (0.08)
NVA single	0.87 (0.21)	0.88 (0.29)	0.82 (0.29)	0.66 (0.20)	0.60 (0.18)	0.61 (0.29)	0.43 (0.18)	0.44 (0.14)	0.65 (0.14)	0.53 (0.10)

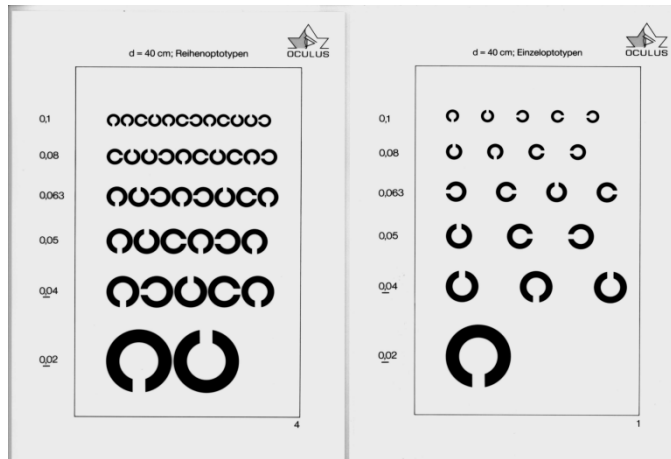
<sup>1</sup> M= magnifier, <sup>2</sup>E= large print, <sup>3</sup>NVA=near visual acuity (crowded=C-test with 2.6', single=C-test with  $\geq 30'$  interoptotype spacing; both at 40cm distance).

The supplementary table provides an overview of the different aetiologies of visual impairment and distance VA of the participants. Overall, 25 children worked with a magnifier (M) and 33 received large print (E). The groups were matched on age and near VA by an independent observer and were statistically equivalent. Both groups were equal in age,  $t(56) = 0.13, p = .896$ , and crowded NVA,  $t(56) = -0.79, p = .433$ . Written consent was obtained from the children's parents. The regional ethics committee (CMO Arnhem Nijmegen) approved the study. The study was conducted in accordance with the Declaration of Helsinki.

### Materials, procedure, and design

All children were examined ophthalmologically before the experiment began. Contrast sensitivity (Kooijman, 1994), mono- and binocular distance VA (Taylor, 1978), visual field, funduscopy and cycloplegia measures were collected. If necessary, the spectacle correction was prescribed or changed before the experiment started. All children with glasses had to wear them during the experiment.

At baseline, NVA was measured with the Landolt C-test at 40 cm without magnification (Haase, 1993; Hohmann & Haase, 1982). The crowded chart had an interoptotype spacing of 2.6', and the single chart had an interoptotype spacing of  $\geq 30'$  at 40 cm (see Figure 4.1). During the experiment, crowded near version was measured with a magnifier or large print (NVA equivalent). A 90 mm diameter glass dome-magnifier was used (Schweizer, Germany, productnr 32090). This magnifier was chosen for several reasons: the large field of view, complete line coverage, and a



**Figure 4.1** Landolt C-test with on the left a crowded page with interoptotype spacing of 2.6' at 40cm, and at the right the single page with interoptotype spacing of at least 30' at 40 cm.

constant magnification factor over different lens-to-object distances (effectively 1.7 $\times$  at 2.5, 10 and 25 cm : Bailey, Bullimore, Greer, & Mattingly, 1994). VI children show large variability in fine motor and navigational skills (Cox, et al., 2009; Reimer, et al., 2011). By choosing this magnifier navigational demands could be excluded as a confounder. The large print group worked with a 1.8 $\times$  copy of the crowded chart. Lighting conditions were controlled by using task light directed to the chart (9000lux close to the chart at 10-15cm and 1300 lux at 40cm from the chart). Children received magnification at the point from where they were no longer able to decipher the crowded optotypes at 40cm without magnification. Children were not allowed to touch the magnifier, but could adopt a self-chosen working distance.

Video-recordings of each experiment were made in order get objective information of the distance between child and the magnifier or large print. Working distances were scored and analysed. Working distance was estimated by two independent raters in cm by using several markers as indicators: height of the magnifier (6 cm), height of the reading standard (30 cm) and hand width (10 cm). Inter-rater reliability was determined using the Kappa statistic.

### Statistical analyses

To investigate the improvement in near vision with magnification, a GLM (Repeated Measures) with near vision without and with magnification (LogMAR) entered as dependent variables. Age group (4-6 years and 7-8 years) and experimental condition (magnifier vs. large print) were entered as between-subjects factors. Separate post-hoc ANOVAs were conducted using Bonferroni statistics to disentangle interaction effects. A univariate ANOVA was conducted to compare response time (the average



time to identify five optotypes) for the magnifier group and the large print group. A hierarchical multiple regression analysis was conducted on improvement of near vision with magnification and response time with the following predictors:

- 1 Age in months;
- 2 Total received magnification: relative size magnification provided by magnifier (2.3 log steps for magnifier and 2.5 for enlarged print)+ relative distance magnification (3 log steps at 20cm, 4.5 at 15 cm, 6 log steps at 10 cm, etc.);
- 3 Crowding score: crowded LogMAR NVA- uncrowded LogMAR NVA (40cm);
- 4 Crowded LogMAR NVA.

Finally, working distance was compared between the two conditions with an independent samples *t*-test. A simple regression analysis was conducted to explore the association between age in months and working distance, VA and working distance, and crowding score and working distance.

## RESULTS

### Near vision

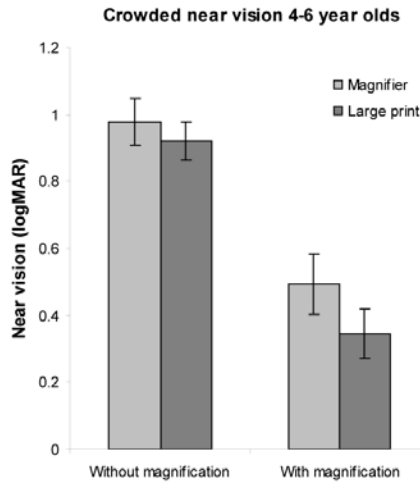
There was a significant interaction between age category and near vision improvement with magnification,  $F(1, 54) = 8.86, p = .004$ , partial  $\eta^2 = .141$ . Therefore, separate analyses were run to examine improvements in both age groups. The 4-6 year-old children showed a significant improvement in near vision with magnification,  $F(1, 30) = 142.52, p < .001$ , partial  $\eta^2 = .826$ . Near vision improved from 0.95 LogMAR ( $SE = .045$ ) without magnification to 0.42 LogMAR ( $SE = .058$ ) with magnification, an improvement of 5.3 log steps. The magnifier group and large print group showed equal improvement,  $F(1, 30) = 1.16, p = .291$ , partial  $\eta^2 = .037$  (see Figure 4.2).

The 7-8 year olds showed a large improvement in near vision with magnification,  $F(1, 24) = 414.65, p < .001$ , partial  $\eta^2 = .945$ . Near vision improved from 0.71 LogMAR ( $SE = .031$ ) without magnification to 0.01 LogMAR ( $SE = .041$ ) with magnification (i.e., 7 log steps). Improvement in near vision did not differ between the two magnification methods,  $F(1, 24) = 1.41, p = .246$ , partial  $\eta^2 = .056$  (see Figure 4.3).

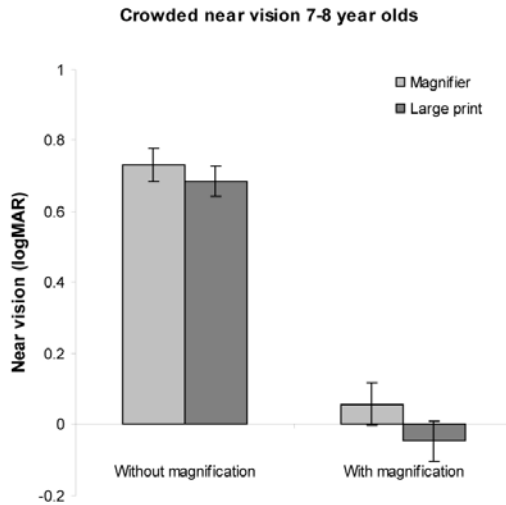
### Response time

Response time decreased with increasing age,  $F(1, 54) = 20.70, p < .001$ , partial  $\eta^2 = .277$ . Average response time to decipher five optotypes was 13.7s ( $SE = 0.8$ ) for 4-to-6 year-old children, and 8.2s ( $SE = 0.9$ ) for 7-to-8 year-old children (Figure 4.4). There was no significant interaction between condition and age,  $F(1, 54) = 1.51, p = .225$ , partial  $\eta^2 = .027$ . Average response time did not differ between the two magnification methods,  $F(1, 54) = 1.05, p = .225$ , partial  $\eta^2 = .027$ . The average

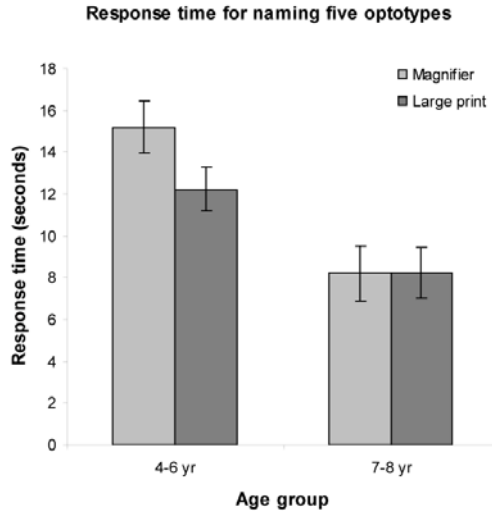
response time was 11.7s ( $SE = 0.9$ ) in the magnifier condition and 10.2s ( $SE = 0.8$ ) in the large print condition.



**Figure 4.2** Crowded near vision (LogMAR) for the 4-6 year old children with magnification and without magnification for the two types of magnification. Error bars represent standard error of the mean (*s.e.m.*).



**Figure 4.3** Crowded near vision (LogMAR) for the 7-8 year old children with magnification and without magnification for the two types of magnification. Error bars represent *s.e.m.*



**Figure 4.4** Response time for naming five optotypes for the two types of magnification. Error bars represent *s.e.m.*

## Regression analysis

### Near vision

The predictors accounted for 36.3% of the variation,  $F(4, 54) = 7.12, p < .001$ . Age, magnification received, and crowding score were significant predictors. Age was the strongest predictor,  $r = .47, t(54) = 4.10, p < .001$ . Total magnification received and crowding score were also significant predictors,  $r = .27, t(54) = 2.08, p = .042$ , and  $r = .29, t(54) = 2.38, p = .021$ , respectively. Crowded NVA was not a significant predictor of the amount of improvement,  $r = -.088, p = .261$ .

### Response time

The predictors accounted for 39.2% of the variation,  $F(4, 54) = 8.07, p < .001$ . Age was the only significant predictor accounting for 37.4% of the variation,  $r = -.61, t(54) = -5.60, p < .001$ . Crowding score and total magnification received did not predict response time,  $r = -.080, p = .280$ , and  $r = -.098, p = .239$ , respectively. Crowded LogMAR NVA and response time correlated moderately,  $r = .233, p = .051$ .

### Working distance

The inter-rater reliability was found to be a Kappa = 0.59 ( $p < .001$ ). There was no difference in working distance between the two groups,  $t(53) = -0.08, p = .940$ . The average working distance was 9.2cm ( $SE = 1.3$ cm) for the magnifier group and 9.3cm ( $SE = 1.2$ cm) for the large print group. Age in months and working distance in cm were not related,  $r = .14, p = .301$ . Crowded LogMAR NVA and working distance

correlated negatively,  $r = -.31$ ,  $p = .022$ . Children with better vision showed larger working distances. There was no association between the crowding score and working distance,  $r = -.11$ ,  $p = .406$ .

## DISCUSSION

The first hypothesis of this study was that children would be equally efficient in deciphering small optotypes on a crowded chart with a magnifier than with large print (with equal magnification factor). The second hypothesis was that the children who experience stronger crowding effects would show more progress on the chart with magnification.

Both hypotheses were confirmed. Four-to-8 year-old VI children are capable of looking through a magnifier adequately at a pre-reading age and do not differ in performance from children who used large print. This new finding on the subject of magnifier use in young children yields new insights in the minimum age at which it is sensible to introduce a low-vision aid to a VI child. The children in the present study had no experience working with a magnifier. Our results implicate that the 90mm dome magnifier was not experienced as an obstruction between the material of interest and the child. The improvement in near vision after using the aid was greater than expected on the basis of the magnification factor of the aid alone and can also be attributed by reducing working distance. Seven-to-8 year-old children showed a larger improvement with magnification than 4-6 year-old children. This difference cannot be explained by shorter working distance employed by the 7-8 year olds, because there was no significant correlation between working distance and age. The most plausible explanation for this larger improvement in older children is greater experience with deciphering small symbols. Children with stronger crowding effects, for whom spacing is suspected to be a bottleneck in object recognition, showed larger improvement with magnification. Our explanation is that the fixed spacing of the Landolt C-test (Huurneman, Boonstra, Cillessen, et al., 2012) is enlarged with magnification and relieves crowding effects for children for whom spacing is crucial (i.e. the constraining factor causing the large discrepancy between crowded and single acuity).

Regression analysis explored which factors predicted the improvement of near vision and response time. Based on earlier work (Lovie-Kitchin, Bevan, & Hein, 2001), age in months, total magnification received, crowding score, and crowded NVA at baseline were employed as predictors of the dependent variables. The regression results were in line with earlier results showing that age significantly predicted performance and reading rate (Lovie-Kitchin, et al., 2001). Baseline crowded NVA did not predict improvement in near vision or response time. Working distance was monitored during the experiment (lens-to-object distance). There was no difference in

self-chosen working distance between the two experimental conditions, nor was there an association between working distance and age. Children with poorer vision adopted a shorter working distance. The magnifier had an equal magnification factor of  $1.7\times$  over a large range of distances (Bailey, et al., 1994). Children showed much variability in their working distance; with this magnifier this did not cause large aberrations. In contrast, magnifiers with stronger lenses have an increasing magnification factor over increasing lens-to-object distances (for example a 24D stand magnifier has magnification factors of  $1.8\times$  at 2.5cm,  $3.3\times$  at 10cm and  $5.6\times$  at 25cm : Bailey, et al., 1994). Thus, when using a stronger lens, the effects of lens-to-object distance on magnification and image seen through the magnifier are stronger.

This experiment focused on comparing two methods of magnification in young VI children. Several useful implications can be drawn from this study. First, there is no difference in task performance between young VI children when working with an optical (dome) magnifier or large print. Not NVA, but age and crowding score, significantly predicted improvement in near vision. The finding that children who experience stronger crowding effects show larger improvement with magnification is interesting and deserves further research. During this experiment, children were allowed to adopt a self-chosen distance. Although we monitored the distance, it would be more informative to control the distance and conduct an experiment in which the association between crowding and magnification could be inspected more carefully. This also is a topic for further research.

## CONCLUSIONS

Four-to-8 year-old VI showed equal crowded task improvement with a magnifier as with large print. VI children as young as 4 years of age are able to use a dome magnifier during near vision tasks (with no imposed navigational demands). Children with stronger crowding effects showed larger improvements. Two direct clinical implications can be drawn from this study. The first is that a large-field dome magnifier is not experienced as an obstruction by the visually impaired child, and is equally effective as large print. The second implication is that children with stronger crowding effects benefit more from magnification. This information is relevant for clinicians prescribing magnification and for professionals working in educational settings with VI children.

## ACKNOWLEDGEMENTS

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**Supplement.** *Aetiologies of visual impairment in VI group and distance visual acuity (LogMAR).*

Child	Age	VA*	Primary diagnosis
110	4	0.70	Congenital Stationary Night Blindness
122	4	0.70	Congenital Stationary Night Blindness
124	4	0.60	Juvenile X-linked retinoschisis
142	4	0.70	Congenital nystagmus
144	4	0.90	Albinism
145	4	1.20	Albinism
150	4	1.10	Albinism
158	4	1.00	Achromatopsia
105	5	1.20	Congenital cataract (aphakia)
113	5	0.60	Juvenile X-linked retinoschisis
118	5	0.45	Congenital Stationary Night Blindness
120	5	1.20	Achromatopsia
125	5	0.60	Juvenile X-linked retinoschisis
130	5	0.70	Albinism
134	5	0.90	Albinism
138	5	0.70	Albinism
143	5	0.60	Congenital nystagmus
146	5	0.60	Juvenile X-linked retinoschisis
152	5	0.70	Hypermetropia (>4 D)
161	5	0.60	Retinitis Pigmentosa
172	5	0.70	Congenital nystagmus
107	6	0.45	Hypermetropia (>4D)
116	6	1.10	Albinism
117	6	0.90	Albinism
123	6	0.45	Albinism, myopia >6D
132	6	0.75	Myopia (high>6D)
136	6	0.45	Congenital nystagmus
141	6	0.90	Congenital cataract (aphakia)
149	6	0.60	Congenital nystagmus
156	6	0.80	Congenital glaucoma
160	6	0.45	Hypermetropia (>4D)
165	6	0.90	Congenital nystagmus
101	7	0.90	Albinism
103	7	0.60	Congenital nystagmus
119	7	0.45	Albinism
121	7	0.45	Albinism, myopia (>6D)
126	7	0.45	Congenital nystagmus
127	7	0.45	Albinism
133	7	0.50	Cone dystrophy, myopia (>6D)
135	7	0.90	Congenital glaucoma
139	7	0.45	Papildysplasia

Crowded task performance: Magnifier versus large print

140	7	0.45	Corneal opacities
147	7	0.45	Congenital Stationary Night Blindness
170	7	0.40	Myopia (>6D)
174	7	0.70	Albinism
109	8	0.75	Congenital cataract (aphakia)
112	8	0.45	Congenital nystagmus
114	8	0.60	Albinism
115	8	0.50	Cone dystrophy, myopia (>6D)
131	8	0.60	Congenital Stationary Night Blindness
154	8	0.50	Congenital Stationary Night Blindness
159	8	0.70	Albinism
163	8	0.60	Juvenile X linked retinoschisis
164	8	0.60	Albinism
167	8	0.90	Congenital Stationary Night Blindness
168	8	0.45	Congenital nystagmus
169	8	0.40	Aniridia
175	8	0.45	Coloboma irides

\* Distance VA as measured with tumbling E's (distance acuity at 6m).

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Crowded visual search in  
children with normal  
vision and children with  
visual impairment

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**ABSTRACT**

This study investigates the influence of oculomotor control, crowding, and attentional factors on visual search in children with normal vision ([NV], n=11), children with visual impairment without nystagmus ([VI-nys], n=11), and children with VI with accompanying nystagmus ([VI+nys], n=26). Exclusion criteria for children with VI were: multiple impairments and visual acuity poorer than 20/400 or better than 20/50. Three search conditions were presented: a row with homogeneous distractors, a matrix with homogeneous distractors, and a matrix with heterogeneous distractors. Element spacing was manipulated in 5 steps from 2-32 minutes of arc. Symbols were sized 2 times the threshold acuity to guarantee visibility for the VI groups. During simple row and matrix search with homogeneous distractors children in the VI+nys group were less accurate than children with NV at smaller spacings. Group differences were even more pronounced during matrix search with heterogeneous distractors. Search times were longer in children with VI compared to children with NV. The more extended impairments during serial search reveal greater dependence on oculomotor control during serial compared to parallel search.

## INTRODUCTION

Children with visual impairment (VI) show weaker visual search performance than children with normal vision (NV) (Tadin, Nyquist, Lusk, Corn & Lappin, 2012). Visual acuity is only moderately related to the degree of visual search performance in observers with VI, indicating that other factors also play a role (MacKeben & Fletcher, 2011, Tadin et al., 2012). In the present study, a visual impairment was defined as having visual acuity equal to or better than 20/400 and equal to or poorer than 20/50. There are at least three factors that can influence visual search performance of children with VI: (i) oculomotor control (MacKeben & Fletcher, 2011), (ii) crowding (the inability to identify target objects when they are surrounded by visual clutter: Whitney & Levi, 2011), and (iii) attention, i.e. the mechanism enabling us to select relevant information out of irrelevant noise (Carrasco, 2011, Carrasco, Ling & Read, 2004). It should be kept in mind that these three factors are interdependent. For example, brain areas involved in visuo-motor modules are also involved in spatial attention networks (Braddick & Atkinson, 2011), and visual search task characteristics (e.g., element spacing) influence oculomotor behaviour (van Zoest, Donk & Theeuwes, 2004, Vlaskamp, Over & Hooge, 2005). Therefore, the aim of this study is not to disentangle the contributions of these factors, but to investigate under which circumstances visual search impairment is greatest in children with VI. The motivation for the present study is to expand our understanding of the (combined) contribution of these factors to impaired visual search performance in children with VI. Besides scientific reasons, this is important in order to develop effective rehabilitation programs for these children.

Poor oculomotor control can set a limitation on visual search performance (Liu, Kuyk & Fuhr, 2007, MacKeben & Fletcher, 2011). The decision of where and when to move the eyes is strongly influenced by the characteristics of the specific search task and the density of the visual array, as well as the viewer strategies (van Zoest & Donk, 2004, van Zoest et al., 2004). The presence of involuntary ocular oscillations (i.e., nystagmus) during visual search might degrade performance, because of the need for refixations after an involuntary eye movement. A large part of the population of children with VI experiences nystagmus due to the presence of an ocular disorder, while there are also children with VI due to 'idiopathic' or 'motor' nystagmus (Fu, Bilonick, Felius, Hertle & Birch, 2011). The degree of fixational instability in nystagmus is correlated with the degradation of visual acuity (Simmers, Gray & Winn, 1999). Up to now, there are no studies in children with VI that have analyzed oculomotor behaviour during visual search, but it is to be expected that search times are longer for children with VI with accompanying nystagmus (VI+nys) due to the need for refixations.

A second factor setting a limit on visual search performance is crowding. Crowding occurs when target perception is deteriorated by the presence of nearby contours or patterns and can be minimized when contours are placed at a distance beyond the threshold at which distractors interfere with target recognition (“critical distance”) (see Levi, 2008, for a review). Visual information from the periphery is used to guide eye movements and a breakdown of this information by crowding can degrade saccadic search (de Vries, Hooge, Wiering & Verstraten, 2011, Vlaskamp & Hooge, 2006). During visual search in adults with NV, decreasing the element spacing to distances smaller than  $1.5^\circ$  causes longer search times, longer fixation durations, more fixations, and smaller saccades (Vlaskamp et al., 2005). In addition to element spacing, stimulus configuration can also influence the strength of the phenomenon. In central vision, surrounding distractors placed above, below and on both lateral sides of the target are more potent elicitors of crowding than laterally placed distractors (Atkinson et al., 1985, Toet & Levi, 1992, Vlaskamp & Hooge, 2006). Increasing object density degrades visual search performance in adults with VI (Dougherty, Martin, Kelly, Jones, Raasch & Bullimore, 2009, Liu et al., 2007). There is evidence that crowding effects are stronger in children with VI than in children with NV at  $8^\circ$  eccentricity (Tadin et al., 2012) and in central vision (Huurneman, Boonstra, Cillessen, van Rens & Cox, 2012a). Furthermore, crowding effects in central vision are even stronger for children with VI+nys than children with VI-nys (Huurneman et al., 2012a). These findings are in line with studies reporting stronger lateral interactions in adults with nystagmus (Chung & Bedell, 1995, Huurneman, Boonstra, Cox, Cillessen & van Rens, 2012b, Pascal & Abadi, 1995). Thus, it might be expected that children with VI, especially children with VI+nys, experience small spacing as a bottleneck during search performance.

Spatial attention is the third limiting factor in visual search tasks (Carrasco, 2011). Search tasks with homogeneous distractors (i.e. parallel search) are considered preattentive, and tasks with heterogeneous distractors (i.e. serial search) require focal attention (Casco, Gidiuli & Grieco, 2000, Treisman & Gelade, 1980). Children from the age of 6 years onwards show improved performance on serial search tasks (Ruskin & Kaye, 1990), which could be related to improvements in attentional top-down control (Hommel, Li & Li, 2004). There is evidence that children with ophthalmic disorder, i.e. children with corrected-to-normal visual acuity, but a history of strabismus, nystagmus or cataract, have attentional impairments as demonstrated by omissions during cancellation tasks and slower execution times than children with NV (Cavezian, Vilayphonh, Vasseur, Caputo, Laloum & Chokron, 2013). As reported above, children with VI show impaired visual search performance (serial search in a wide-field naturalistic display) and stronger peripheral crowding effects, which might both be caused by limited attentional resolution (Carrasco, 2011, Tadin et al., 2012).

Because of the reported attentional impairments of children with VI, these children might show disproportionately poor performances on serial tasks compared to children with NV.

The contribution of the above mentioned factors on visual search performance will be investigated in three visual search tasks. The role of oculomotor control is investigated by comparing performance of children with VI+nys with children with VI-nys or NV. The role of crowding is investigated by manipulating element spacing and stimulus configuration (row versus matrix search). Finally, homogeneous and heterogeneous distractors were used so as to manipulate attentional load during task performance. Three hypotheses were evaluated: (i) children with VI+nys show poorer performance than children with NV on visual search tasks with small element spacing, (ii) there are no group differences in the row configuration, but children with VI are expected to show weaker performance than children with NV in the matrix configuration with homogeneous distractors, and (iii) children with VI show a disproportionately poor search performance on serial tasks compared to children with NV.

## **METHODS**

### **Participants**

Eleven children with NV, 11 children with VI without nystagmus (VI-nys), and 26 children with VI with accompanying nystagmus (VI+nys) participated. Inclusion criteria for all groups were: (a) age between 6 and 8 years, (b) normal developmental level, (c) birth at term ( $\geq 36$  weeks of gestation), and (d) birth weight  $\geq 3000$  grams. Inclusion criteria for the children with VI was visual acuity between 20/400 and 20/50. Exclusion criteria were the presence of multiple impairments and/or central scotomas. Table 5.1 presents the characteristics of the children (age, distance visual acuity, and near visual acuity). Clinical characteristics of patients can be found in Table 5.2. Children with NV were included from regular primary schools in the Netherlands. Children with VI were included from client databases of all Dutch vision rehabilitation centres. Written consent was obtained from the parents of the participants. A local ethics committee approved the study before the assessments were conducted (CMO Arnhem Nijmegen). The study was conducted in accordance with the Declaration of Helsinki.

### **Ophthalmological examination**

All children were examined ophthalmologically before the experiment started. Visual acuity was measured binocularly at 6 m with the tumbling E-chart at 6m (Taylor, 1978) under controlled lighting conditions. Near visual acuity was determined with the LH-version of the C-test at 40 cm, which contains a crowded version with

**Table 5.1.** *Characteristics of children with normal vision (NV), children with visual impairment without nystagmus (VI-nys), and children with VI with accompanying nystagmus (VI+nys). Mean age, distance and near visual acuity (decimal notation), and near visual acuity as determined with the staircase method are given. Numbers in parentheses are standard deviations.*

	NV	VI-nys	VI+nys
Age in months	92 (12)	90 (11)	90 (10)
N	11	11	26
DVA*	1.17 (0.08)	0.28 (0.12)	0.25 (0.10)
NVA**	1.70 (0.38)	0.41 (0.14)	0.35 (0.16)
NVA staircase	n.a.	0.42 (0.14)	0.35 (0.14)

\* Distance Visual Acuity (DVA) measured with E-gratings at 6 m.

\*\* Near Visual Acuity (NVA) measured with LH-single symbols at 40 cm.

interoptotype spacing of 2.6' (' refers to minutes of arc) and an uncrowded version with interoptotype spacing of at least 30' (Haase & Hohmann, 1982, Huurneman et al., 2012a, Hyvarinen, Nasanen & Laurinen, 1980). A gross estimation of the visual field was obtained by confrontational techniques. Testing central visual fields was not yet possible in these young children. However in near vision tasks there were no signs of central scotomas. Objective refraction was obtained after cycloplegia and if necessary the spectacle correction was prescribed or changed before the experiment started. Children with glasses had to wear them during the entire study.

### Procedure

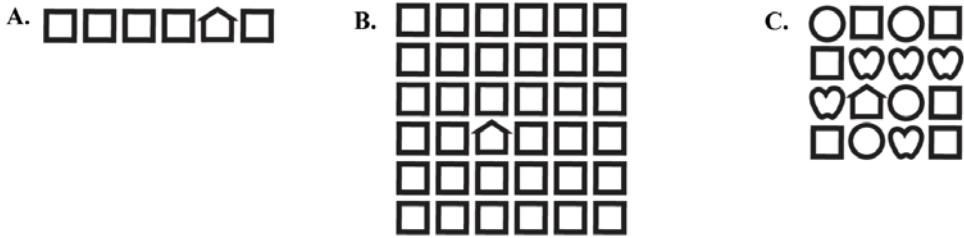
Children sat at a distance of 60 cm from the monitor wearing their best available optical correction. Viewing was binocular. Before the children performed the search tasks, a three-up one-down 75% correct threshold stair-case method was used to determine the smallest identifiable LH-symbol (house, square, circle and apple; Hyvarinen et al., 1980). Three visual search conditions were presented with symbols at double the threshold size, so as to guarantee visibility for the children with VI (MacKeben & Fletcher, 2011). For children with VI-nys the average symbol size was 0.57°, and for the children with VI+nys this was 0.67°. Children with NV served as a control group and were presented with the same size symbols as the children with VI+nys (0.67°). Two simple search tasks with homogeneous distractors and one complex search task with heterogeneous distractors were presented (see Fig. 5.1). The instruction in all search tasks was to identify the unique symbol. The location of the unique symbol was randomly varied to make sure the child had to actively search for it. Tasks were presented in block form in random order. The influence of crowding was measured by manipulating spacing, with edge-to-edge element spacing at 2', 4', 8', 16' and 32'. Four trials were presented at every spacing for each task, giving 20 trials



**Table 5.2** *Causes of visual impairment in the two patient groups.*

<b>Children with visual impairment without nystagmus</b>		
<b>ID</b>	<b>Clinical diagnosis</b>	<b>Binocular DVA*</b>
115	Cone dystrophy	0.30
121	Oculocutaneous albinism	0.36
127	Oculocutaneous albinism	0.36
133	Cone dystrophy	0.30
135	Congenital glaucoma	0.12
140	Corneal opacities	0.36
147	Congenital Stationary Night Blindness	0.36
156	Congenital glaucoma	0.15
160	Hypermetropia (>4D)	0.36
170	Myopia (>6D)	0.40
175	Coloboma irides	0.36
<b>Children with visual impairment with accompanying nystagmus</b>		
<b>ID</b>	<b>Clinical diagnosis</b>	<b>Binocular DVA*</b>
101	Albinism	0.12
103	Congenital nystagmus	0.24
107	Hypermetropia (>4D)	0.36
109	Congenital cataract (aphakia)	0.18
112	Congenital nystagmus	0.36
114	Albinism	0.24
116	Albinism	0.08
117	Albinism	0.12
119	Albinism	0.36
123	Albinism	0.36
126	Congenital nystagmus	0.36
131	Congenital Stationary Night Blindness	0.24
132	Myopia (>6D)	0.18
136	Congenital nystagmus	0.36
139	Papildysplasia	0.36
141	Congenital cataract (aphakia)	0.12
149	Congenital nystagmus	0.24
154	Congenital Stationary Night Blindness	0.30
159	Albinism	0.20
163	Juvenile X-linked retinoschisis	0.24
164	Albinism	0.24
165	Congenital nystagmus	0.12
167	Congenital Stationary Night Blindness	0.12
168	Congenital nystagmus	0.36
169	Aniridia	0.40
174	Albinism	0.20

per task, adding up to a grand total of 60 trials in the experiment. Spacing was fixed for the visual search tasks. This in line with research reporting that charts with fixed spacing are most sensitive to pick up crowding effects (Graf, Becker & Kaufmann, 2000, Haase & Hohmann, 1982, Huurneman et al., 2012a). Each next trial was presented after the child pressed the response button on the button box.



**Table 5.1** Examples of the visual search stimuli: [A] row with homogeneous distractors, [B] matrix with homogeneous distractors, and [C] matrix with heterogeneous distractors.

**Apparatus**

Stimuli were generated by a Windows XP computer and presented on a 17-inch TFT monitor with integrated eye-trackers (Tobii T120, Tobii Corporation, Danderyd, Sweden). Stimulus presentation was driven by custom-written Delphi code provided by the scientific programmer of our research institute. We did not fix the head positions of the children. A rule was incorporated into the stimulus-presentation software to assure that the children were seated at a proper viewing distance. When children came closer to the monitor than 60 cm, the stimulus disappeared from the screen, and reappeared if they were seated at 60 cm or more again. This rule was included to prevent children from reducing their viewing distance, as well as to standardize our measurements. Eye movements were registered at 60 Hz sampling rate. Before the visual search tasks were presented, a standard 5-point eye-tracker calibration procedure was performed for both eyes. Fixations were detected offline and were defined as periods in which eye velocity remained below an adaptively determined threshold for at least 50 ms. The velocity threshold was calculated as 3.5 times the standard deviation of the eye velocity below 25°/sec and was recalculated for each session.

**Statistical analysis**

The presentation of results is divided into two sections: [1] Effects of homogeneous distractors on target detection, and [2] Effects of heterogeneous distractors on target detection. Visual search performance was quantified by two dependent variables: accuracy, defined as the mean percentage of correct responses (i.e. the total count of

correct trials divided by the total number of trials), and search time, defined as the mean response latency for correct trials. Eye-movement data were used when eye movements were correctly recorded in at least 60% of the total recording time for each trial. The data of children with less than 10 valid trials per condition were removed. The following dependent variables were measured: number of fixations (mean), fixation duration (mean), and saccade amplitude (mean).

We used nonparametric statistical tests (Kruskal-Wallis for between-group effects and Friedman's tests for within-group effects of spacing), because of unequal variances and skewed distributions. Post-hoc tests were conducted by making pairwise comparisons. A correction for pairwise comparisons (Type 1 errors) was made by reporting the adjusted p-value in which the  $K$  refers to the number of groups ( $p_{adj} = p * K(K-1)/2$ ; Daniels, 1990).

A partial correlation analysis was conducted to investigate relations between oculomotor and performance measures in the VI+nys group while controlling for visual acuity. This analysis was conducted for the VI+nys group, because of special interest between oculomotor control and search performance. The relations between the following variables was investigated for simple matrix search and complex matrix search with spacing of 2': accuracy, search time, crowding ratio (i.e. the ratio of single acuity and line acuity (Pardhan, 1997)), number of fixations, fixation duration, and saccade amplitude.

## RESULTS

### Effect of homogeneous distractors

#### Performance measures: accuracy and search times

Results are shown in Fig. 5.2-5.4. A complete overview of descriptive and test statistics of performance measures is reported in supplement S1; here, we only report statistically significant results. Groups differed in accuracy: children in the VI+nys group showed lower accuracies than children in the NV group during row (at 2' and 8';  $p$ 's <0.05; Fig. 5.2A) and matrix search (at 2' and 4';  $p$ 's <0.05; Fig. 5.3A). Spacing only affected accuracy during matrix search in children in the VI+nys group. They were less accurate at smaller spacings than larger spacings (2', 4' < 16', 32',  $p$ 's <0.05; Fig. 5.3A).

Search times were about 2 times longer during row search and up to 5-fold longer for matrix search for children with VI than children with NV ( $p$ 's <0.01; Fig. 5.2B and 5.3B). Spacing also affected search times: children in the NV group were quicker at smaller spacings during row search (2', 4' < 8', 32',  $p$ 's <0.1; Fig. 5.2B) and slower at the smallest spacing during matrix search (2' > 16', 32',  $p$ 's <0.1; Fig. 5.3B). Children in the VI+nys group were slower at 4' than 8' during row search. Children in both VI groups

were slower at smaller spacings during matrix search (VI-nys:  $2' > 4'-32'$ ,  $p's < 0.05$ ; VI+nys:  $2', 4' > 8'-32'$ ,  $p's < 0.1$ ; Fig. 5.3B).

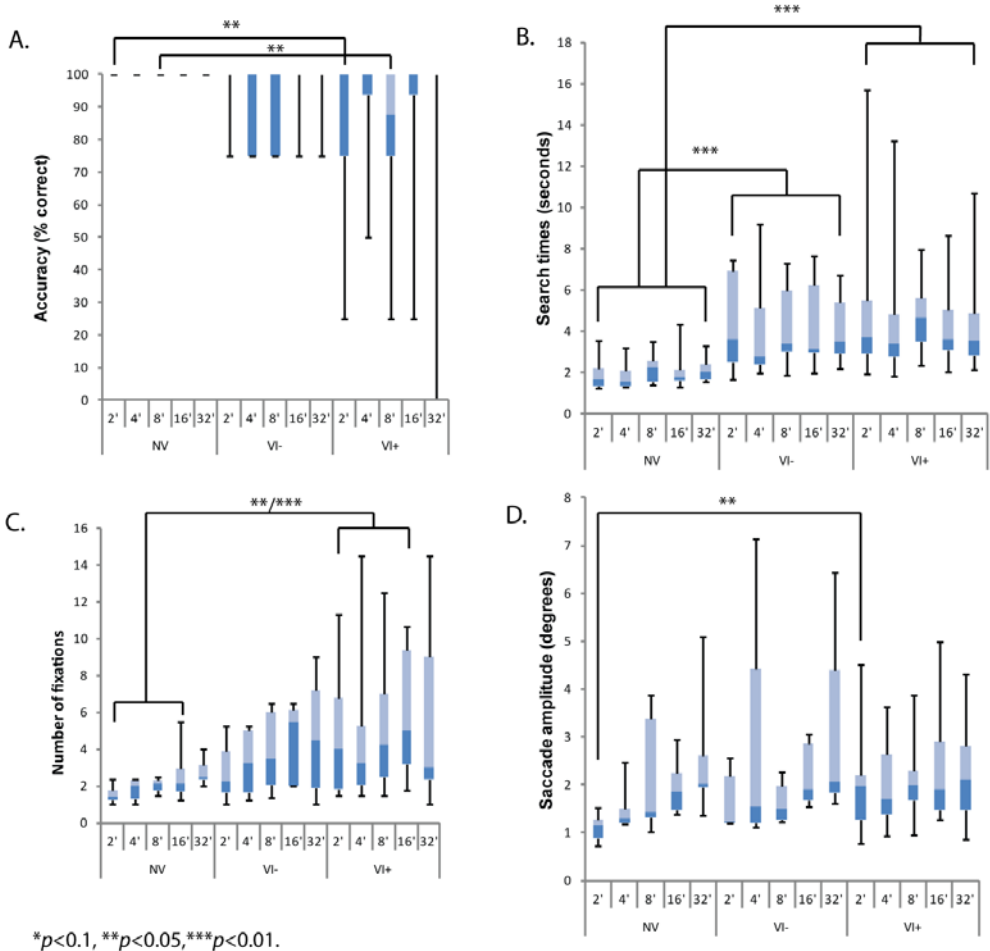
In sum, children in the VI+nys group showed lower accuracies at smaller spacings during simple row and matrix search than children in the NV group. In addition, search times were up to 5-fold longer for children in the VI groups compared to children in the NV group.

### 3.1.2. Eye movements

Statistics of eye movements are reported in the supplementary table S2. We collected 29 valid eye-movement recordings for row search (NV: 8; VI-nys: 5; VI+nys: 16), and 28 valid recordings for matrix search (NV: 9; VI-nys: 4; VI+nys: 15). Groups differed in number of fixations during simple row search: children in the VI+nys group made more fixations than children in the NV group, except at  $32'$  ( $p's < 0.05$ ; Fig. 5.2C). During simple matrix search there were more pronounced group differences: children in both VI groups made more fixations than children in the NV group (VI+nys all spacings,  $p's < 0.01$ ; Fig. 5.3C; VI-nys  $2', 8'$ , and  $32'$ ,  $p's < 0.05$ ; Fig. 5.3C). Spacing influenced number of fixations during row search only in children in the NV group: they made fewer fixations at  $2'$  than  $32'$  spacing ( $p < 0.01$ ; Fig. 2C). In contrast, children in the VI+nys group made more fixations at smaller spacings during matrix search ( $p's < 0.01$ ; Fig. 5.3C). No within-subject effects were found for the children in the VI-nys and NV group during simple matrix search ( $p's > 0.12$ ).

During row search children in the VI-nys group fixated longer than children in the VI+nys group at the smallest spacing ( $p's < 0.1$ ), and tended to fixate longer than children with NV at the largest spacing ( $p's < 0.1$ ). Spacing influenced fixation duration of children in the VI+nys group during matrix search: they fixated longer at smaller spacings ( $p's < 0.05$ ; S2). Although there was a main effect of spacing on fixation duration in children in the NV group, there were no significant post-hoc effects (S2). Saccade amplitudes did differ between groups during row search: saccade amplitudes were larger at  $2'$  for children in the VI+nys group than children in the NV group (medians resp.  $2.0^\circ$  and  $1.2^\circ$ ,  $p < 0.05$ ; Fig. 5.2D). Spacing influenced saccade amplitude during row and matrix search in children with NV: they made smaller saccades at smaller spacings ( $p's < 0.05$ ; Fig. 5.2D). Children in the VI+nys group made smaller saccades at  $4'$  than  $32'$  during matrix search ( $p < 0.05$ ; Fig. 5.2D).

Summarizing, children with VI made more fixations than children with NV during simple matrix search and only children in the VI+nys group needed more fixations at the smaller compared to larger spacings (see Fig. 5.4). Children in the VI+nys group also made more fixations than children in the NV group during simple row search. Group differences in number of fixations during simple row search disappeared when



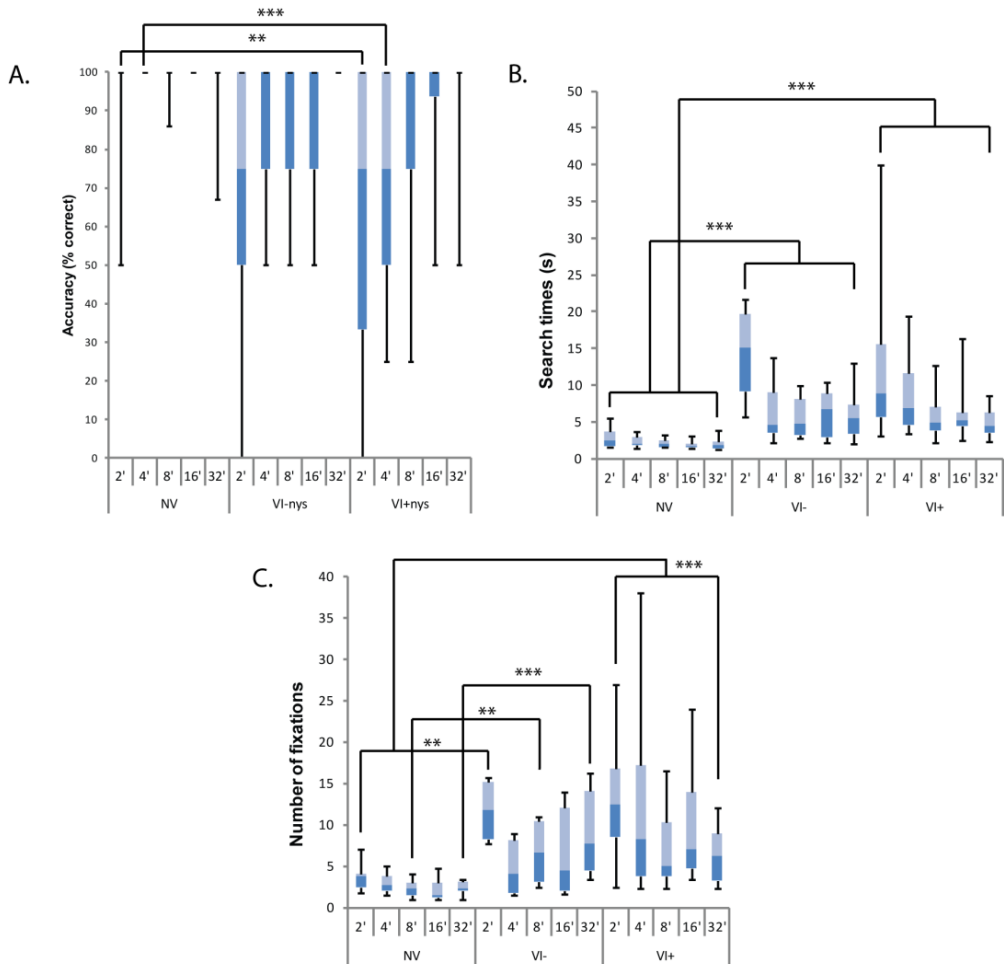
**Figure 5.2.** Box-whisker plots for the distribution of dependent variables in the **row configuration**: [A] accuracies, [B] search times, [C] number of fixations, and [D] saccade amplitudes. The categories on the X-axis are the experimental groups: children with normal vision (NV), with visual impairment without nystagmus (VI-), and with visual impairment showing nystagmus (VI+) and the stimulus spacings. Boxes and whiskers: quartiles and range, respectively.

spacing was 32'. Finally, children in the VI+nys group showed larger saccade amplitudes than children with NV at 2' spacing during simple row search.

### Effect of heterogeneous distractors

#### Performance measures: accuracy and search times

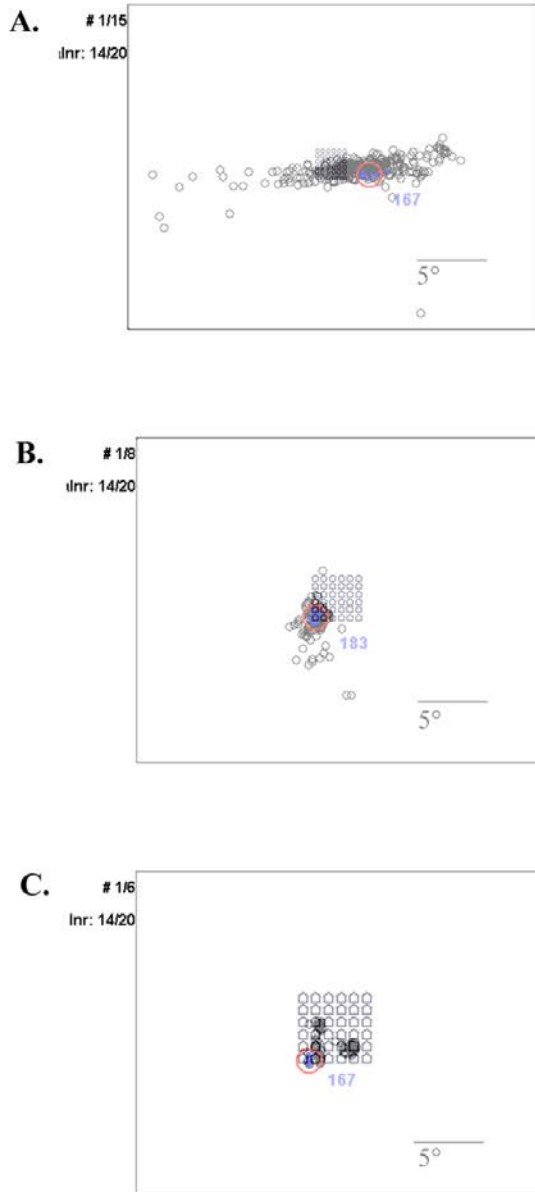
During complex matrix search groups differed in accuracy: children in the VI+nys group were less accurate than children in the NV group until at least 16' ( $p$ 's < 0.05; Fig.



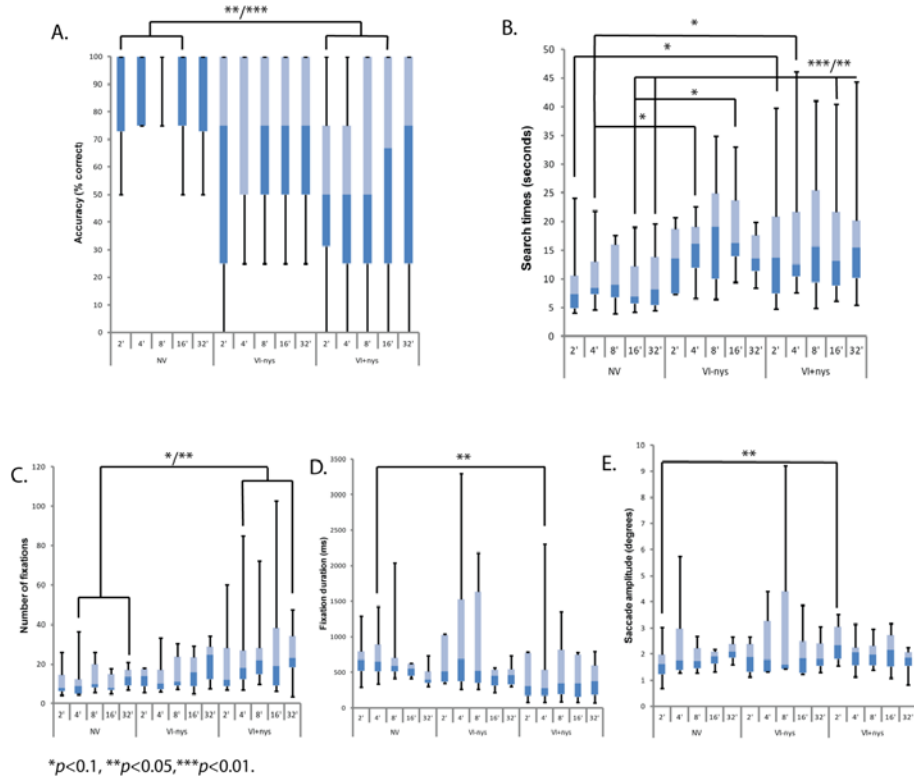
\* $p < 0.1$ , \*\* $p < 0.05$ , \*\*\* $p < 0.01$ .

**Figure 5.3** Box-whisker plots for the distribution of dependent variables in the **matrix configuration**: [A] accuracies, [B] search times, [C] number of fixations. The categories on the X-axis are representative of groups: children with normal vision (NV), with visual impairment without nystagmus (VI-), and with visual impairment showing nystagmus (VI+). Boxes and whiskers: quartiles and range, respectively.

5.5A). Although there was a main effect of spacing on performance in the VI+nys group, there were no significant post hoc effects (S1). Search times for children with VI+nys were longer than for children with NV at all spacings except at 8' ( $p$ 's < 0.1; Fig. 5.5B). Children in the VI-nys group tended to be slower than children in the NV group at 4' and 16' spacing ( $p$ 's < 0.1; Fig. 5.5B). Search times were unaffected by spacing ( $p$ 's > 0.17).



**Figure 5.4** Raw plots containing all fixation points for: [A] a child with visual impairment showing nystagmus, [B] a child with visual impairment without nystagmus, [C] a child with normal vision (same trial). The two children with visual impairment gave incorrect answers. The child with normal vision gave a correct answer. As can be seen, the child with normal vision has small clusters of fixation points. The two children with visual impairment show less defined fixation clusters.



**Figure 5.5** Box-whisker plots for the distribution of dependent variables in the matrix configuration: [A] accuracies, [B] search times, [C] number of fixations, [D] fixation duration, and [E] saccade amplitudes. The categories on the X-axis are representative of groups: children with normal vision (NV), and with visual impairment without nystagmus (VI-), and with visual impairment showing nystagmus (VI+). Boxes and whiskers: quartiles and range, respectively.

### Eye movements

We collected 26 valid eye-movement recordings (NV: 10; VI-nys: 6; VI+nys: 10). Children in the VI+nys group made more fixations than children in the NV group from 4' until 32' ( $p < 0.1$ ; Fig. 5.5C). None of the groups were affected by spacing ( $p > 0.22$ ). Groups also differed in fixation duration: children with VI+nys fixated shorter than children with NV (at 4': medians 278 ms vs. 658 ms,  $p < 0.05$ ; Fig. 5.5D). Only children in the NV group adjusted their fixation duration to spacing by fixating longer at smaller spacings ( $p < 0.05$ ; Fig. 5.5D). There were no within-subjects effects of spacing on fixation duration in the VI groups ( $p > 0.29$ ). Finally, group differences appeared for saccade amplitude. As was the case during simple row search, children in the VI+nys group made larger saccades than children in the NV group at the smallest



spacing (at 2': medians 2.3° and 1.6°,  $p < 0.05$ ; Fig. 5.5E). Saccade amplitude was not influenced by spacing in any of the groups ( $p$ 's  $> 0.20$ ; see S2).

### Correlations between search performance and oculomotor measures

Accuracy and search times during simple matrix search were not related to the crowding ratio or any of the oculomotor measures (see Table 5.3). The only significant relation that was observed was a negative relation between the number of fixations made and the crowding ratio,  $r = -0.58$ . During complex visual search, accuracy was negatively related to the crowding ratio and was positively related to the saccade amplitude. Search times were negatively related to crowding ratios and showed a positive relation with number of fixations and fixation duration. Crowding ratios were only related to accuracy for serial search performance, and not for parallel search performance.

**Table 5.3** *Correlations between performance measures, crowding ratio, and oculomotor measures for simple and complex matrix search with 2' spacing. The matrix displays partial correlations for the VI+nys group while controlling for visual acuity.*

Complex Simple	Accuracy	Search time	Crowding ratio	#Fixations	Fixation duration	Saccade amplitude
Accuracy		0.17	-0.66*	-0.10	0.47	0.86**
Search time	-0.06		-0.65*	0.67*	0.70*	-0.02
Crowding ratio	0.23	0.31		-0.52	-0.38	-0.58
# Fixations	-0.07	-0.22	-0.58*		0.10	-0.05
Fixation duration	-0.23	0.17	-0.15	-0.02		0.14
Saccade amplitude	0.26	-0.26	0.28	-0.32	-0.16	

\* $p < 0.05$ , \*\* $p < 0.01$  (one tailed  $p$ -test).

## DISCUSSION

In this study, the following three hypotheses were evaluated: (i) children in the VI+nys group show poorer performance than children in the NV group on visual search tasks with homogeneous distractors and small element spacing, (ii) there are no group differences in the row configuration, but children with VI are expected to show

weaker performance than children with NV in the matrix configuration with homogeneous distractors, and (iii) children with VI show a disproportionately poor search performance on serial search tasks compared to children with NV. Error rates were high for the VI+nys group (especially during trials with small spacings), but there were no statistically significant differences in search time for correct and incorrect trials in the VI+nys group (Friedman's test), e.g. medians simple matrix search 2 minutes of arc: 8.9s for correct trials and 6.4s for incorrect trials,  $p=0.62$ . Therefore, the VI+nys group appears to be slower compared to the NV group regardless of the correctness of trials and search times seem to be representative for this group.

### **The influence of nystagmus on visual search tasks with homogeneous distractors**

The first hypothesis was confirmed: children in the VI+nys group showed poorer performance on search tasks with homogeneous distractors and small element spacing than children with NV. Children in this group showed lower accuracies than children in the NV group at smaller spacings during row and matrix search. Search times were longer during simple search tasks with largest group differences occurring at small element spacings.

Our first explanation for the weaker search performance of children in the VI+nys group compared to children in the NV group is weaker oculomotor control. We found two group differences in oculomotor recordings: (i) children in the VI+nys group made more fixations than children with NV, and (ii) children in the VI+nys group showed larger saccade amplitudes than children in the NV group at 2' spacing in two out of three conditions. The oculomotor strategy found in children in the VI+nys group, i.e. making more fixations and larger saccadic amplitudes, deviates from the strategy observed in children with NV in the present study and in previous studies in subjects with normal oculomotor control reporting smaller saccade amplitudes at smaller spacings (Vlaskamp & Hooge, 2006, Vlaskamp et al., 2005). This adaptation of oculomotor strategy in children in the VI+nys group might be best explained by motor aspects that are characteristic for this group (i.e., the presence of involuntary ocular oscillations) and less from visual aspects. The oculomotor strategy we found in children in the VI+nys group has not been reported before but has been found in adults with amblyopia (more refixations during reading: Kanonidou, Proudlock & Gottlob, 2010; larger saccade amplitudes: Shi, Xu, Li, Wang, Zhao & Sabel, 2012).

A second explanation for the weaker performance might be found in the lack of experience with these kinds of tasks and the predictability of the task. For example, reading speed of adults with infantile nystagmus syndrome does not differ from that of adults with NV (Barot, McLean, Gottlob & Proudlock, 2013, Thomas, Gottlob,

McLean, Maconachie, Kumar & Proudlock, 2011). Eye movement data demonstrated that adults with infantile nystagmus syndrome learn to compensate for their nystagmus using a range of strategies. These strategies include taking advantage of the stereotypical and periodic nature of the involuntary eye movements to achieve the desired goal by their means (Thomas et al., 2011). However, the oculomotor strategies observed in adults with nystagmus may be resulting from experience with the expected voluntary behaviour of the eyes accumulated over many years during visual development. Such experience is obviously much less in the group of children included in our study.

### **Differences between row and matrix search with homogeneous distractors**

The second hypothesis was partially confirmed. We expected that there would be no group differences in the row configuration, but that children with VI show weaker performance than children with NV in the matrix configuration with homogeneous distractors. The first part of our hypothesis was not confirmed: we actually did find group differences during row search. Children with VI+nys showed lower accuracies than children with NV, but there were no (within-subjects) effects of spacing on accuracy. The second part of our hypothesis was confirmed: children in the VI+nys did show lower accuracies and children in both VI groups did show longer search times than children with NV at smaller spacings. This effect was stronger in the matrix than in the row configuration. During row search, spacing did not influence search time and accuracy of the children with VI and small spacings even facilitated search in children with NV (i.e. shorter search times at smaller element spacing). This latter finding is in line with studies indicating that patterns with discriminable elements in close proximity can be segregated more easily than patterns in which the same elements are more widely spaced (Nothdurft, 1985, Nothdurft, 1993, Scolari, Kohnen, Barton & Awh, 2007).

An explanation for the weaker performance of the VI groups compared to the NV group during matrix search is to be sought in their lower acuity and the larger need for refixations. The partial correlations show that performance measures during simple matrix search were not significantly related to any of the oculomotor or crowding measures when controlling for acuity. The stimulus should be visible for the children with VI, because the stimulus was presented at twice the size of their threshold acuity. However, this might not be enough for the children with VI. This is in line with recent studies on reading, which report that the difference in reading acuity (smallest readable print size) and critical print size (font size below which reading is suboptimal) is 0.3 log units, i.e. factor 2, in children and adults with albinism and up to 0.6 log units, i.e. factor 4, in adults with nystagmus (Barot et al., 2013, Merrill, Hogue, Downes, Holleschau, Kutzbach, MacDonald & Summers, 2011). The crowding ratio

was not related to accuracy for simple matrix search performance ( $r=-0.23$ ), but the crowding ratio was related to accuracy during complex matrix search ( $r=-0.66$ ).

A second explanation for the weaker search performance during matrix search might be masking. Masking is distinct from crowding and considered as a loss of visual information within the visual system, and crowding effects are more complex phenomena including contour interactions (a type of lateral masking), attentional factors, and fixational eye movements (Flom, 1991). Tasks that require single feature detection are immune, or nearly so, to crowding (Pelli et al., 2004). Masking could occur during trials where the only unique target feature was located at the upper or lower site of the target (e.g., search for house surrounded by squares or vice versa). This explanation would provide an answer for: (i) the lower accuracies during small spacings in matrix search (and the lack of spacing effects during row search), and (ii) the striking drop in accuracy at the two smallest spacings. However, there was no difference in accuracy or search times between trials with unique features at the lower or upper site and trials in which targets share no features with distractors (for example, a square target between apple distractors). While our analysis does not support this masking hypothesis, future research is warranted to identify the underlying mechanisms and ideally includes a task measuring target recognition with simple flanking bars to rule out simple masking effects as an explanation.

In sum, our findings are in line with earlier research demonstrating that crowding effects are stronger for surrounding distractors placed above, below, and on both sides of the target than laterally placed distractors (Atkinson et al., 1985). Search performance was degraded by smaller element spacing during simple matrix search in all groups (manifested by longer search times), but caused greater impairment for children in the VI+nys group.

### **Differences between search with homogeneous and heterogeneous distractors**

Our third hypothesis was confirmed: children with VI did show disproportionately poor search performance on serial search tasks compared to children with NV. This might be explained by the lack of a perceptual phenomenon called distractor-distractor grouping during search with heterogeneous distractors which is known to reduce or release crowding effects (for a review: Whitney & Levi, 2011). When distractors are grouped separately from the target, as might occur during search with homogeneous distractors, crowding effects can be reduced. In the task with heterogeneous distractors, distractors could not be grouped. Because crowding was stronger, more than twice the number of fixations were required and accuracies were lower compared to homogeneous search (in line with Ruskin & Kaye, 1990).

A second explanation for the extended group differences in the matrix with heterogeneous distractors, is the greater dependence on accurate eye movements

during serial compared to parallel search (Young & Hulleman, 2013). And indeed, relations between oculomotor measures and performance measures were found even while controlling for acuity. Accuracy was negatively related to the crowding ratio ( $r=-0.66$ ), and saccade amplitude was positively related to accuracy ( $r=0.86$ ). This unexpected relation between saccade size and accuracy might be due to the need to re-inspect earlier visited areas. Search time was positively related to the number of fixations ( $r=0.67$ ) and fixation duration ( $r=0.70$ ). The crowding ratio was negatively related to search time ( $r=-0.65$ ).

We suspect that our finding is the result of an inability of the children with VI+nys to adjust saccade size and to fixate steadily, because oculomotor control appears to play a larger role when elements in a display have to be scrutinized in a serial manner. While a consistent adaptation of fixation duration and saccade amplitude was observed in the children with NV, we did not observe these adaptive abilities as strongly in our VI groups. From this perspective, oculomotor control can be seen as a prerequisite to perform a complex search tasks with small symbols. The lower accuracies were probably not caused by attentional impairments, because group differences in accuracy disappeared at 32' element spacing in all three search tasks. The lower accuracies of children with VI+nys were relieved by increasing element spacing, thus spacing poses a bottleneck for performance in children with VI+nys. This is in line with the outcome of the correlation analysis which shows that the crowding ratio showed a strong relation with accuracy during complex search. Thus, oculomotor control is related to performance on untrained search tasks, especially when there is a need for accurate fixational eye movements and densely spaced elements have to be disentangled.

## CONCLUSIONS

The present work indicates that children with VI (with and without nystagmus) show longer search times on visual search tasks with homogeneous distractors compared to children with NV. The difference between groups is larger for matrix search than for row search. Furthermore, children with VI+nys showed lower accuracies on search tasks with homogeneous distractors than children with NV at the smallest spacings, and group differences increased for matrix search with heterogeneous distractors. Group differences in accuracy disappeared at the largest element spacing. Visual search performance is weaker when distractors surround the target in all directions than when distractors only surround the target laterally. A practical implication that can be extracted from this study is that increasing vertical interline spacing, or introducing a typoscope which isolates 1 or 2 lines on a page (Rowe & VIS group UK, 2011), could be beneficial for children with VI.

## **ACKNOWLEDGEMENTS**

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**Table S1.** Summary of the performance measures grouped by task and spacing.

Accuracy	Medians			Group differences ( $\chi^2$ statistic)	Pairwise comparisons	Within-subjects effects			
	NV	VI-nys	VI+nys			NV	VI-nys	VI+nys	
Simple row	2'	1.00	1.00	$\chi^2(2)=6.89$ , $p=0.032$	VI+nys<NV**	$\chi^2(4)=0$ , $p=1.00$	$\chi^2(4)=4.36$ , $p=0.359$	$\chi^2(4)=9.03$ , $p=0.060$ . Post-hoc n.s.	
	4'	1.00	1.00	$\chi^2(2)=3.20$ , $p=0.202$	n.s.				
	8'	1.00	1.00	$\chi^2(2)=8.47$ , $p=0.014$	VI+nys<NV**				
	16'	1.00	1.00	$\chi^2(2)=3.69$ , $p=0.158$	n.s.				
	32'	1.00	1.00	$\chi^2(2)=2.77$ , $p=0.250$	n.s.				
Simple matrix	2'	1.00	0.75	$\chi^2(2)=7.37$ , $p=0.025$	VI+nys<NV**	$\chi^2(4)=3.50$ , $p=0.478$	$\chi^2(4)=15.2$ 4, $p=0.004$ . Post-hoc n.s.	$\chi^2(4)=31.4$ 6, $p=0.000$ . Post-hoc: 2'<16'**,32' *** 4'<16'**, 32'***	
	4'	1.00	0.75	$\chi^2(2)=12.30$ , $p=0.002$	VI+nys<NV***				
	8'	1.00	1.00	$\chi^2(2)=2.60$ , $p=0.272$	n.s.				
	16'	1.00	1.00	$\chi^2(2)=3.32$ , $p=0.190$	n.s.				
	32'	1.00	1.00	$\chi^2(2)=1.31$ , $p=0.518$	n.s.				
Complex matrix	2'	1.00	0.50	$\chi^2(2)=9.65$ , $p=0.008$	VI+nys<NV***	$\chi^2(4)=4.05$ , $p=0.400$	$\chi^2(4)=2.32$ , $p=0.677$	$\chi^2(4)=9.54$ , $p=0.049$ . Post-hoc n.s.	
	4'	1.00	0.50	$\chi^2(2)=13.32$ , $p=0.001$	VI+nys<NV***				
	8'	1.00	0.50	$\chi^2(2)=13.10$ , $p=0.001$	VI+nys<NV***				
	16'	1.00	0.75	$\chi^2(2)=6.61$ , $p=0.037$	VI+nys<NV**				
	32'	1.00	0.75	$\chi^2(2)=3.80$ , $p=0.150$	n.s.				
Search times	Medians			Group differences ( $\chi^2$ statistic)	Pairwise comparisons	Within-subjects effects			
	NV	VI-nys	VI+nys			NV	VI-nys		VI+nys
	Simple row	2'	1.6	3.6	$\chi^2(2)=17.91$ , $p=0.000$	VI-nys=VI+nys>NV***	$\chi^2(4)=16.15$ , $p=0.003$ . Post-hoc: 2'<8'* 4'<8', 32'***	$\chi^2(4)=2.62$ , $p=0.624$	$\chi^2(4)=9.15$ , $p=0.057$ Post-hoc: 4'<8'*
		4'	1.5	2.8	$\chi^2(2)=19.01$ , $p=0.000$	VI-nys=VI+nys>NV***			
		8'	2.2	3.4	$\chi^2(2)=18.78$ , $p=0.000$	VI-nys=VI+nys>NV***			
		16'	1.8	3.1	$\chi^2(2)=14.25$ , $p=0.001$	VI-nys=VI+nys>NV***			
		32'	2.0	3.5	$\chi^2(2)=18.47$ , $p=0.000$	VI-nys=VI+nys>NV***			
	Simple matrix	2'	2.5	15.1	$\chi^2(2)=24.40$ , $p=0.000$	VI-nys=VI+nys>NV***	$\chi^2(4)=12.51$ , $p=0.014$ . Post-hoc:	$\chi^2(4)=19.4$ 7, $p=0.001$ . Post-hoc:	$\chi^2(4)=40.7$ 4, $p=0.000$ .
		4'	2.0	4.6	$\chi^2(2)=24.50$ , $p=0.000$	VI-nys=VI+nys>NV***			
		8'	2.0	4.7	$\chi^2(2)=22.31$ , $p=0.000$	VI-nys=VI+nys>NV***			

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16'	1.7	6.8	5.2	$\chi^2(2)=22.53, p=0.000$	VI-nys=VI+nys>NV***	$2'>16^*$ , $32^{**}$	$2'>4'$ , $8^{***}$ , $16', 32^{**}$	Post-hoc: $2'$ , $4'>8^{***}/*$ , $16^{***}/$ , $32^{***}/***$
32'	1.8	5.6	4.5	$\chi^2(2)=22.81, p=0.000$	VI-nys=VI+nys>NV***			
Complex matrix 2'	7.4	13.6	13.7	$\chi^2(2)=5.40, p=0.067$	VI+nys>NV*		$\chi^2(4)=4.00$ , $p=0.406$	$\chi^2(4)=4.21$ , $p=0.378$ .
4'	8.4	16.1	12.5	$\chi^2(2)=6.28, p=0.043$	VI-nys=VI+nys>NV*			
8'	9.0	19.1	15.6	$\chi^2(2)=4.75, p=0.093$	n.s.			
16'	6.9	16.3	13.1	$\chi^2(2)=10.86, p=0.004$	VI-nys=VI+nys>NV*/***			
32'	8.2	13.6	15.5	$\chi^2(2)=7.84, p=0.020$	VI+nys>NV**			

\* $p<0.1$ , \*\* $p<0.05$ , \*\*\* $p<0.01$ .



**Table S2.** *Summary of eye movements grouped by task and spacing.*

Number of fixations	Medians			Group difference ( $\chi^2$ statistic)	Pairwise comparison	Within subjects effects			
	NV	VI-nys	VI+nys			NV	VI-nys	VI+nys	
Simple row	2'	1.42	2.25	4.00	$\chi^2(2)=9.56, p=0.008$	VI+nys>NV***	$\chi^2(4)=14.45, p=0.006$ Post-hoc: 2'<32'***	$\chi^2(4)=8.96, p=0.062$ Post hoc n.s.	$\chi^2(4)=9.87, p=0.043$ Post-hoc n.s.
	4'	2.00	3.25	3.25	$\chi^2(2)=6.59, p=0.037$	VI+nys>NV**			
	8'	2.13	3.50	4.25	$\chi^2(2)=7.30, p=0.026$	VI+nys>NV**			
	16'	2.13	5.50	5.00	$\chi^2(2)=7.73, p=0.021$	VI+nys>NV**			
	32'	2.50	4.50	3.00	$\chi^2(2)=2.31, p=0.315$	n.s.			
Simple matrix	2'	3.75	11.75	12.50	$\chi^2(2)=12.57, p=0.002$	VI-nys=VI+nys>NV**/ ***	$\chi^2(4)=7.09, p=0.131$	$\chi^2(4)=7.20, p=0.126$	$\chi^2(4)=18.84, p=0.001$ Post-hoc: 2'>8'***, 32'*** 16'>8'***, 32'*
	4'	2.75	4.00	8.25	$\chi^2(2)=10.43, p=0.005$	VI+nys>NV***			
	8'	2.25	6.63	5.00	$\chi^2(2)=13.46, p=0.001$	VI-nys=VI+nys>NV**/ ***			
	16'	1.50	4.50	7.00	$\chi^2(2)=15.71, p=0.000$	VI+nys>NV***			
	32'	2.25	7.75	6.25	$\chi^2(2)=13.74, p=0.001$	VI-nys=VI+nys>NV***			
Complex matrix	2'	7.75	13.71	12.00	$\chi^2(2)=3.56, p=0.169$	n.s.	$\chi^2(4)=5.65, p=0.227$	$\chi^2(4)=4.67, p=0.323$	$\chi^2(4)=5.20, p=0.267$
	4'	9.00	10.00	18.00	$\chi^2(2)=6.99, p=0.030$	VI+nys>NV**			
	8'	9.75	11.13	21.92	$\chi^2(2)=5.98, p=0.050$	VI+nys>NV*			
	16'	7.88	15.75	19.12	$\chi^2(2)=5.20, p=0.074$	VI+nys>NV*			
	32'	13.50	24.63	23.08	$\chi^2(2)=6.98, p=0.030$	VI+nys>NV**			
Fixation duration	Medians (ms)			Group difference ( $\chi^2$ -statistic)	Pairwise comparison	Within subjects effects			
	NV	VI-nys	VI+nys			NV	VI-nys	VI+nys	
Simple row	2'	378	768	252	$\chi^2(2)=5.25, p=0.072$	VI-nys>VI+nys*	$\chi^2(4)=13.10, p=0.011$ Post-hoc: 2', 8' >32'***	$\chi^2(4)=5.28, p=0.260$	$\chi^2(4)=2.95, p=0.566$
	4'	433	507	305	$\chi^2(2)=2.06, p=0.357$	n.s.			
	8'	356	467	314	$\chi^2(2)=5.08, p=0.079$	n.s.			
	16'	398	432	275	$\chi^2(2)=2.40, p=0.301$	n.s.			
	32'	218	442	287	$\chi^2(2)=5.99, p=0.050$	VI-nys>NV*			

Simple matrix	2'	322	622	348	$\chi^2(2)=1.63, p=0.442$	n.s.	$\chi^2(4)=9.78, p=0.044$ Post-hoc n.s.	$\chi^2(4)=7.00, p=0.136$	$\chi^2(4)=23.47, p=0.000$ Post-hoc: 2' > 16'**, 32'*** 4' > 16'*, 32'*** 8' > 32'***
	4'	344	499	338	$\chi^2(2)=1.14, p=0.567$	n.s.			
	8'	336	363	267	$\chi^2(2)=0.16, p=0.992$	n.s.			
	16'	265	353	267	$\chi^2(2)=1.61, p=0.447$	n.s.			
	32'	225	327	282	$\chi^2(2)=1.74, p=0.419$	n.s.			
Complex matrix	2'	681	516	314	$\chi^2(2)=3.48, p=0.175$	n.s.	$\chi^2(4)=11.20, p=0.024$ Post-hoc: 2' > 32'*, 4' > 32'***	$\chi^2(4)=4.93, p=0.294$	$\chi^2(4)=4.00, p=0.406$
	4'	659	689	278	$\chi^2(2)=7.60, p=0.022$	VI+nys < NV**			
	8'	591	525	351	$\chi^2(2)=2.77, p=0.251$	n.s.			
	16'	556	454	347	$\chi^2(2)=2.41, p=0.299$	n.s.			
	32'	405	460	378	$\chi^2(2)=0.41, p=0.817$	n.s.			
Saccade amplitude	Medians (degrees)		Group difference ( $\chi^2$ statistic)		Pairwise comparison		Within subjects effects		
		NV	VI-nys	VI+nys			NV	VI-nys	VI+nys
Simple row	2'	1.15	1.23	1.97	$\chi^2(2)=7.57, p=0.023$	VI+nys > NV**	$\chi^2(4)=14.90, p=0.005$ Post-hoc: 2' < 16'*, 32'***	$\chi^2(4)=8.96, p=0.062^*$ Post-hoc n.s.	$\chi^2(4)=8.15, p=0.086$ Post-hoc n.s.
	4'	1.30	1.55	1.69	$\chi^2(2)=3.67, p=0.159$	n.s.			
	8'	1.42	1.50	2.00	$\chi^2(2)=2.49, p=0.287$	n.s.			
	16'	1.86	1.90	1.89	$\chi^2(2)=0.39, p=0.822$	n.s.			
	32'	2.02	2.05	2.10	$\chi^2(2)=0.49, p=0.784$	n.s.			
Simple matrix	2'	2.20	1.92	2.14	$\chi^2(2)=0.66, p=0.718$	n.s.	$\chi^2(4)=16.71, p=0.002$ Post-hoc: 2' < 32'*, 8', 16' < 32'***	$\chi^2(4)=8.20, p=0.085$ Post-hoc n.s.	$\chi^2(4)=10.67, p=0.031$ Post hoc: 4' < 32'***
	4'	2.31	1.25	1.86	$\chi^2(2)=2.00, p=0.367$	n.s.			
	8'	3.13	1.93	2.02	$\chi^2(2)=3.59, p=0.166$	n.s.			
	16'	1.68	1.51	1.92	$\chi^2(2)=3.29, p=0.193$	n.s.			
	32'	3.00	1.87	2.23	$\chi^2(2)=4.32, p=0.115$	n.s.			
Complex matrix	2'	1.62	1.89	2.34	$\chi^2(2)=6.27, p=0.044$	VI+nys > NV**	$\chi^2(4)=5.36, p=0.252$	$\chi^2(4)=2.00, p=0.736$	$\chi^2(4)=5.92, p=0.205$
	4'	1.76	1.78	2.08	$\chi^2(2)=0.08, p=0.963$	n.s.			
	8'	1.75	1.60	1.98	$\chi^2(2)=0.55, p=0.759$	n.s.			
	16'	1.90	1.84	2.16	$\chi^2(2)=0.98, p=0.612$	n.s.			
	32'	2.10	1.82	1.86	$\chi^2(2)=2.63, p=0.269$	n.s.			

\* $p < 0.1$ , \*\* $p < 0.05$ , \*\*\* $p < 0.01$ .

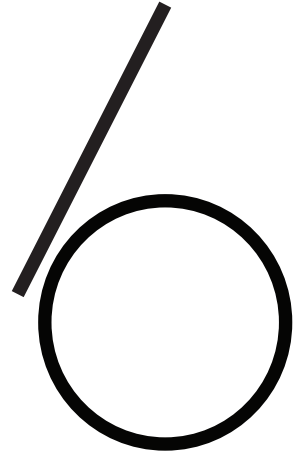
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Monocular and binocular  
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## ABSTRACT

**Background/aims:** To compare interocular acuity differences, crowding ratios, and binocular summation ratios in 4-8 year old children with albinism (n=16), children with infantile nystagmus syndrome (n=10), and children with normal vision (n=72).

**Methods:** Interocular acuity differences and binocular summation ratios were compared between groups. Crowding ratios were calculated by dividing the single Landolt C decimal acuity with the crowded Landolt C decimal acuity mono- and binocularly. A linear regression analysis was conducted to investigate the contribution of five predictors to the monocular and binocular crowding ratio: nystagmus amplitude, nystagmus frequency, strabismus, astigmatism, and anisometropia.

**Results:** Crowding ratios were higher under mono- and binocular viewing conditions for children with infantile nystagmus syndrome than for children with normal vision. Children with albinism showed higher crowding ratios in their poorer eye and under binocular viewing conditions than children with normal vision. Children with albinism and children with infantile nystagmus syndrome showed larger interocular acuity differences than children with normal vision (0.1 LogMAR in our clinical groups and 0.0 LogMAR in children with normal vision). Binocular summation ratios did not differ between groups. Strabismus and nystagmus amplitude predicted the crowding ratio in the poorer eye ( $p=0.015$  and  $p=0.005$ , respectively). The crowding ratio in the better eye showed a marginally significant relation with nystagmus frequency and depth of anisometropia ( $p=0.082$  and  $p=0.070$ , respectively). The binocular crowding ratio was not predicted by any of the variables.

**Conclusions:** Children with albinism and children with infantile nystagmus syndrome show larger interocular acuity differences than children with normal vision. Strabismus and nystagmus amplitude are significant predictors of the crowding ratio in the poorer eye.



## INTRODUCTION

Children and adults with normal vision (NV) show better acuity scores when measured under binocular than monocular viewing circumstances (Masgoret, Asper, Alexander, & Suttle, 2011; Vedamurthy, Suttle, Alexander, & Asper, 2007). If the acuities of two eyes are equal, binocular performance is better than monocular performance, a phenomenon called binocular summation (Blake, 1973; Masgoret, Asper, Alexander, & Suttle, 2010). In normal development, the binocular summation ratio decreases with increasing age, due to slow development of visual acuity of the dominant eye (Vedamurthy, et al., 2007).

In certain populations binocular summation is absent. Individuals with amblyopia experience inhibitory interaction when two eyes are stimulated simultaneously (Vedamurthy, et al., 2007). In the case of inhibitory interaction, binocular acuity is worse than monocular acuity of the dominant eye. Interocular differences of only 1D to 2D are associated with amblyopia effects in children and the severity of the suppression correlates with the magnitude of the anisometropia (Barrett, Candy, McGraw, & Bradley, 2005; Bharadwaj & Candy, 2011; Donahue, 2005; Fielder & Moseley, 1996). In terms of interocular acuity differences, 2 or more LogMAR lines are an indicator of amblyopia (Dobson, Miller, Clifford-Donaldson, & Harvey, 2008). In the past, several kinds of amblyopia have been identified: strabismic, anisometric, nystagmus, and deprivation amblyopia (Haase, 1993). Visual crowding, defined as worse line acuity compared to single acuity, is a characteristic symptom of amblyopia (Graf, et al., 2000; Haase, 1993). Several studies have reported larger interocular acuity differences and a high incidence of amblyopia in adults with infantile nystagmus syndrome (INS) (Hertle, Yang, Adams, & Caterino, 2011; McLean, Proudlock, Thomas, Degg, & Gottlob, 2007). Individuals with strabismic amblyopia experience the strongest crowding effects (in the amblyopic eye: Haase, 1993).

Children with ocular disorders have a higher risk of developing strabismus than children without ocular disorder (Rydberg, et al., 1999). The prevalence of strabismus among children with INS and children with albinism has been reported to be 17% and 53%, respectively (Brodsky & Fray, 1997). Adults with INS show larger contour interaction areas than adults with NV (Chung & Bedell, 1995; Simmers, et al., 1999). Crowding effects are stronger in adults with INS than in adults with NV and the difference between adults with albinism and adults with NV was not significant (Pascal & Abadi, 1995). The incessant image motion can result in a form of sensory amblyopia (Chung & Bedell, 1995). The amblyopia presumably is a consequence of the incessant image motion coupled, in many cases, with sizeable astigmatic refractive errors during the period of visual plasticity in early life (Bedell & Loshin, 1991). Thus,

stronger crowding effects in adults with INS have been associated with decreased foveation time (Pascal & Abadi, 1995), and with the presence of additional (astigmatic) amblyopia effects (Chung & Bedell, 1995). Furthermore, there is a high prevalence of strabismus in children with idiopathic INS and children with albinism (Brodsky & Fray, 1997). We will investigate the contribution of these factors on monocular and binocular crowding ratios in children with albinism, INS and NV.

This work compares mono- and binocular development measures in children with albinism, children with INS, and children with NV. The first hypothesis is that interocular acuity differences will be larger in children with albinism and INS than in children with NV. The second hypothesis is that crowding ratios will be higher in the poorer eye of children with albinism and INS than in children with NV. The third hypothesis is that children with NV show higher binocular summation ratios than children with albinism or INS.

## **MATERIALS AND METHODS**

### **Participants**

Participants were 72 children with NV, 16 children with albinism, and 10 children with INS. Inclusion criteria were: age 4 to 8 years, normal developmental level (no intellectual impairments),  $\geq 36$  weeks of gestation, and birth weight of  $\geq 3000$  grams. Distance visual acuity was 20/50 or less ( $\geq 0.40$  LogMAR) for children with albinism and children with INS. Children with NV had distance visual acuities of 20/25 or better ( $\leq 0.10$  LogMAR). Exclusion criteria were intellectual and/or motor impairments and the presence of central scotomas. Children with NV came from regular primary schools in the Netherlands. Children with albinism or INS came from client databases of all Dutch vision rehabilitation centres. The project was approved by an accredited Medical Ethics Review Committee (CMO-Arnhem Nijmegen) and the protocol adhered to the tenets of the Declaration of Helsinki. Table 6.1 presents the characteristics of the three groups (age, and distance visual acuities). There were no age differences between the three groups,  $F(2, 97) = 0.105$ ,  $p = 0.900$ . Clinical characteristics of the children with albinism and INS can be found in the supplement. Nystagmus characteristics (frequency and amplitude) were measured under binocular viewing conditions using data from the left eye with a Tobii Eye-tracker (Tobii T120, Tobii Corporation, Danderyd, Sweden; sampling rate 60Hz).

### **Ophthalmological examination**

All children underwent ophthalmological examination. Distance visual acuity was measured monocularly and binocularly with the tumbling E-chart at 6m

**Table 6.1** Characteristics of children with normal vision and visually impaired children (*n*, age (months), and distance visual acuity (DVA) in LogMAR (decimal visual acuity). Plus-minus sign represents standard deviations. DVAs=distance visual acuity single (interoptotype spacing  $\geq 30'$  at 5m), DV Au=distance visual acuity uncrowded (interoptotype spacing 17.2' at 5m), DVAc=distance visual acuity crowded (interoptotype spacing 2.6' at 5m).

		Normal vision	Albinism	Nystagmus
<b>n</b>		72	16	10
<b>Age</b>		80.8± 14.2	79.1± 17.6	79.8± 13.2
<b>DVAs</b>	<b>Binocular</b>	-0.08± 0.05 (1.20)	0.69± 0.25 (0.24)	0.54± 0.10 (0.29)
	<b>Better eye</b>	-0.07±0.05 (1.19)	0.71±0.22 (0.22)	0.55±0.10 (0.29)
	<b>Poorer eye</b>	-0.04±0.08 (1.11)	0.84±0.25 (0.18)	0.64±0.11 (0.24)
<b>DVAu</b>	<b>Binocular</b>	-0.08± 0.05 (1.21)	0.76± 0.27 (0.21)	0.60± 0.09 (0.25)
	<b>Better eye</b>	-0.08±0.05 (1.21)	0.80±0.30 (0.19)	0.60±0.11 (0.26)
	<b>Poorer eye</b>	-0.05±0.08 (1.15)	0.91±0.31 (0.15)	0.76±0.17 (0.19)
<b>DVAc</b>	<b>Binocular</b>	0.01± 0.10 (1.05)	0.86± 0.33 (0.18)	0.70± 0.06 (0.20)
	<b>Better eye</b>	0.01±0.10 (0.99)	0.88±0.34 (0.17)	0.73±0.08 (0.19)
	<b>Poorer eye</b>	0.05±0.12 (0.93)	1.02±0.32 (0.12)	0.81±0.09 (0.16)

(Taylor, 1978), and the C-test at 5m (Haase & Hohmann, 1982). Stereo-vision was assessed with the Titmus Fly Test (Hasche, Gockeln, & de Decker, 2001). Strabismus was detected with the cover-uncover test. The diagnosis of the children was confirmed by a standardized ophthalmologic investigation, including ophthalmic, general and family history. Clinical ophthalmological examinations were performed by experienced ophthalmologists; slit lamp examination of the anterior segment and fundus examination in full mydriasis. If necessary Optical Coherence Tomography (OCT), Visual Evoked Potentials (VEP) on misrouting or genetic analysis were performed to confirm the diagnosis. The C-test consisted of three versions: 1) a single chart version with interoptotype spacing of at least 30' at 5m, 2) an uncrowded version with interoptotype spacing of 17.2' at 5m, and 3) a crowded version with interoptotype spacing of 2.6' at 5m. The experiment was conducted in a room with ambient lighting of 76-148 cd/m<sup>2</sup>. Children were asked to identify 5 symbols per row and could progress to the next line if they identified 3 or more of the 5 symbols correctly. If there were less than 5 symbols on a row, children progressed if they correctly identified at least half of the symbols.

Objective refraction was obtained after cycloplegia; if necessary the spectacle correction was prescribed or changed before the experiment started. All children with glasses had to wear them during the experiment.

### Statistical analysis

The nonparametric Kruskal-Wallis test was used to investigate group differences, because of skewed distributions and unequal variances. A correction for pairwise comparisons was made by reporting the adjusted  $p$ -value in which the  $K$  refers to the number of groups ( $p_{\text{adj}}=p*K(K-1)/2$ ) (Daniels, 1990). Three measures were compared:

- Interocular acuity differences:  $\Delta$  better eye and poorer eye (LogMAR);
- Bino- and monocular crowding ratios: single acuity/crowded acuity (Huurneman, Boonstra, Cillessen, et al., 2012);
- Binocular summation ratios: visual acuity measured binocularly (VAB)/ visual acuity measured monocularly in the better eye (VAB/VAM: Pardhan, 1993).

A linear regression analysis was conducted for the mono- and binocular crowding ratios with five predictors: nystagmus amplitude (continuous variable), nystagmus frequency (continuous variable), strabismus (categorical variable; 0=absent, 1=present), astigmatism (continuous variable;  $\Delta$  dioptres of cylindrical refraction between the two eyes) and anisometropia (continuous variable;  $\Delta$  dioptres of spherical refraction between the two eyes). In this analysis only the children with albinism and those with INS were included. A second linear regression analysis was conducted for both clinical groups separately with the two strongest predictors to investigate whether the results depend on the patient group assessed.

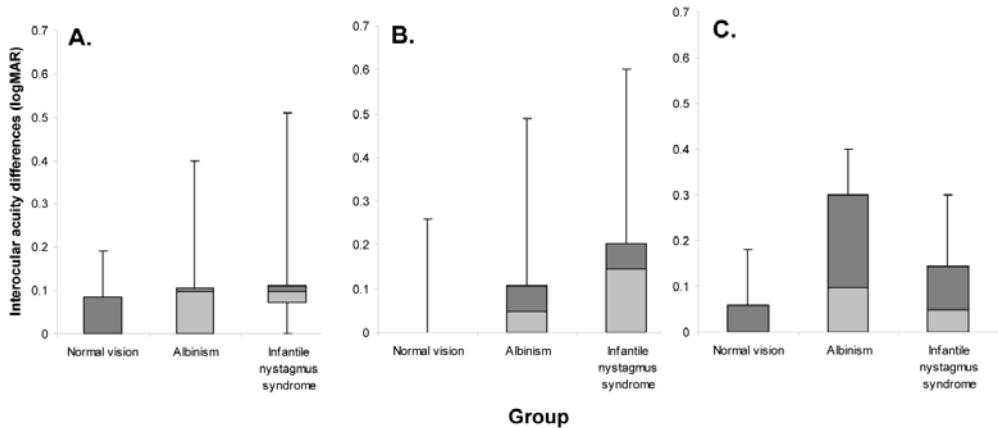
## RESULTS

### Interocular acuity differences

**Single (spacing  $\geq 30'$  at 5m).** Interocular acuity differences for the single chart differed across groups ( $\chi^2(2) = 14.093, p = 0.001$ ). Children with albinism and children with INS had significantly larger interocular acuity differences (medians 0.10 LogMAR) than children with NV (median 0 LogMAR) ( $p= 0.025$  and  $p=0.007$ , respectively). Figure 6.1A represents the interocular acuity differences for the single chart.

**Uncrowded (spacing 17.2' at 5m).** Interocular differences also differed for the uncrowded chart ( $\chi^2(2) = 15.981, p < 0.001$ ). Children with albinism and children with INS (medians 0.05 and 0.15 LogMAR) showed larger interocular acuity differences than children with NV (median 0 LogMAR) ( $p=0.044$  and  $p=0.001$ , respectively). Figure 6.1B represents the interocular acuity differences for the uncrowded chart.

**Crowded (spacing 2.6' at 5m).** There was no difference between groups for the interocular differences measured with the crowded chart ( $\chi^2(2) = 5.871, p = 0.053$ ). The crowded interocular acuity difference was 0.10 LogMAR for children with albinism, 0.05 LogMAR for children with INS, and 0 LogMAR for children with NV (see Figure 6.1C). There were 6 children with albinism and 2 children with INS with



**Figure 6.1** Box-whisker plots for the distribution of interocular acuity differences as measured with: [A.] the single chart (spacing of at least 30' at 5m), [B] the uncrowded chart (spacing of 17.2' at 5m), and [C] the crowded chart (spacing of 2.6' at 5m). Boxes and whiskers: quartiles and range, respectively.

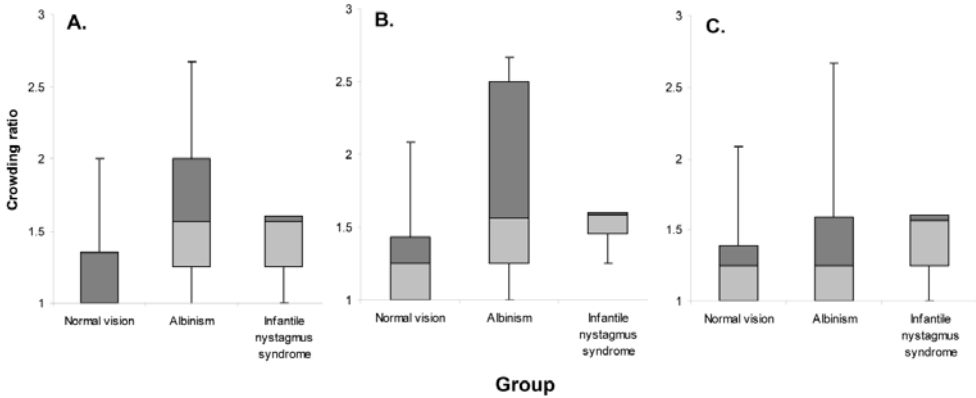
interocular acuity differences of 2 or more log steps on the crowded chart (see Table 6.2), whereas this difference was never reached in the children with NV.

### Crowding ratio

**Binocular crowding.** Groups differed in binocular crowding ratios ( $\chi^2(2) = 18.197, p < 0.001$ ). Crowding ratios were higher for children with albinism and children with INS (medians 1.56) than children with NV (median 1.00) ( $p=0.002$  and  $p=0.006$ , respectively). Figure 6.2A represents the binocular crowding ratio.

**Poorer eye.** Groups also differed in crowding ratios for the poorer eye ( $\chi^2(2) = 19.179, p < 0.001$ ). Again, crowding ratios were higher for children with albinism and children with INS (medians 1.56 and 1.58) than children with NV (median 1.25) ( $p=0.002$  and  $p=0.004$ , respectively). Figure 6.2B represents the crowding ratio of the poorer eye.

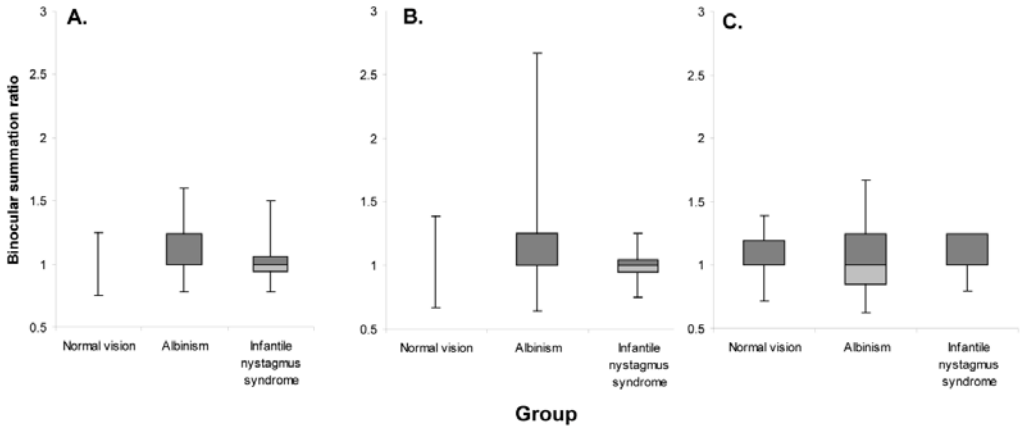
**Better eye.** Groups also differed in crowding ratios in the better eye ( $\chi^2(2) = 8.248, p=0.016$ ). With this comparison, children with INS had significantly higher crowding ratios (median 1.56) in their better eye than children with NV (median 1.25) ( $p=0.013$ ). There was no difference between median crowding ratio in the better eye of children with albinism (median 1.25) and children with NV or INS ( $p=1.000$  and  $p=0.159$ , respectively). Figure 6.2C represents the crowding ratio of the better eye.



**Figure 6.2** Box-whisker plots for the distribution of: [A] the binocular crowding ratio, [B] the crowding ratio in the poorer eye, and [C] the crowding ratio in the better eye. Boxes and whiskers: quartiles and range, respectively.

**Binocular summation ratio**

No binocular summation was observed in any of the groups. Neither the single, nor the uncrowded, nor the crowded binocular summation ratio differed between groups ( $\chi^2(2) = 0.460, 1.985, \text{ and } 0.207$ , respectively,  $p=0.795, p=0.371, \text{ and } p=0.902$ , respectively). The medians for all groups and all charts were 1.00 (see Figure 6.3).



**Figure 6.3** Box-whisker plots for the distribution of: [A] the binocular summation ratio for the single chart, [B] the binocular summation ratio for the uncrowded chart, and [C] the binocular summation ratio for the crowded chart. Boxes and whiskers: quartiles and range, respectively.

**Table 6.2** *Children with  $\geq 2$  log steps interocular acuity differences on the crowded chart.*

#	Age	Diagnosis	Refraction	Deviation	IADc **	CR* ** bino	CR poorer eye	CR better eye	Binocular summation	Better eye
114	8	Oculocutaneous albinism	R S:+7.25 C:-4.25 L S:+7.00 C:-3.75	R esotropia	3 log steps	1.25	2.50	1.25	0.80	L
116	6	Oculocutaneous albinism	No correction	R esotropia	3 log steps	1.56	2.50	1.60	0.80	L
121	7	Oculocutaneous albinism	No correction	orthophoria	4 log steps	0.63	1.00	0.80	1.00	R
134	5	Oculocutaneous albinism	R S: plan C:-1.75 L S: plan C:-1.00	L esotropia	3 log steps	1.25	2.50	1.00	1.00	L
150	4	Ocular albinism	R S:+4.25 C:-2.00 L S:+4.75 C:-2.00	R exotropia	3 log steps	2.00	2.50	1.00	0.63	L
174	7	Oculocutaneous albinism	R S:+3.50 C:-0.75 L S: plan C: plan	orthophoria	3 log steps	1.00	1.50	1.25	1.25	L
103	7	INS*	R S:-2.25 C:-0.75 L S:-1.75 C:-0.25	orthophoria	3 log steps	1.25	1.60	1.00	0.80	L
126	7	INS	R S:+4.25 C:-3.00 L S:+4.50 C:-3.25	L esotropia	2 log steps	1.60	1.60	1.60	1.00	R

\* INS= Infantile nystagmus syndrome

\*\* IADc= Interocular Acuity Differences crowded

\*\*\* CR= Crowding Ratio

### Predictors of crowding

**Poorer eye.** Our predictors showed no strong correlation with each other (see Table 6.3). One child with albinism was removed from this part of the analysis due to the presence of a latent nystagmus in the right eye. Nystagmus characteristics were based on recordings of the left eye, and these characteristics are therefore not representative for the poorer (right) eye of this child. The predictors together accounted for 54.9% of the variance in the crowding ratio of the poorer eye ( $F(5, 17)=4.136, p=0.012$ ). Nystagmus amplitude was the strongest predictor of the crowding ratio in the poorer eye ( $t=3.268, p=0.005$ ). Strabismus also significantly influenced the crowding ratio in the poorer eye ( $t=2.708, p=0.015$ ). The other three predictors did not exert a significant influence on the crowding ratio in the poorer eye (see Table 6.4).

**Better eye.** The predictors together accounted for 26.7% of the variance in the crowding ratio of the better eye ( $F(5, 18)=1.309, p=0.304$ ) (see Table 6.4). When looking at the contribution of the individual variables, it can be seen that nystagmus frequency and anisometropia exerted a marginally significant influence on the crowded ratio in the better eye ( $t=1.843, p=0.082$ , and  $t=1.930, p=0.070$ , respectively).

**Binocular.** The predictors together accounted for 27.3% of the variance in the binocular crowding ratio ( $F(5, 18)=1.349, p=0.289$ ). None of the predictors showed a significant (or marginally significant) relation with the binocular crowding ratio (see Table 6.4).

**Table 6.3** Correlation matrix of predictors and crowding ratios (CR=crowding ratio).

	Nystagmus amplitude	Nystagmus frequency	Strabismus	Astigmatism	Anisometropia	CR poorer eye	CR better eye
Nystagmus frequency	-0.14						
Strabismus	-0.07	-0.00					
Astigmatism	0.03	-0.29	-0.35*				
Anisometropia	-0.08	-0.27	0.11	0.12			
CR poorer eye	0.55**	-0.19	0.48**	-0.10	-0.02		
CR better eye	0.12	0.28	-0.12	-0.06	0.26	0.25	
CR bino	0.28	0.16	0.09	-0.28	0.19	0.46**	0.66**

Note. \*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$  (one-tailed  $p$ -test).

### Results per patient group

The contribution of the two strongest predictors was evaluated in our two clinical groups (see Table 6.5 for a correlation matrix). In the group with albinism, the predictors (nystagmus amplitude and strabismus) accounted for 65.6% of the total variance in the crowding ratio of the poorer eye ( $F(2,11)=10.500, p=0.003$ ). In the group with nystagmus, the predictors (nystagmus frequency and strabismus)



accounted for 50.5% of total variance ( $F(2, 6)=3.056, p=0.122$ ). The crowding ratio of the better eye and binocular crowding ratio were not predicted by the variables (albinism:  $F(2, 12)=1.643, p=0.234$ , and  $F(2, 12)=1.671, p=0.229$ , respectively; INS:  $F(2, 6)=1.817, p=0.242$ , and  $F(2, 6)=1.922, p=0.226$ , respectively).

**Table 6.4** Predictors of the monocular and binocular crowding ratios.  $R^2$  refers to the percentage of variance that can be accounted for by the predictors. Beta refers to the standardized regression coefficient.

	Crowding ratio poorer eye	Crowding ratio better eye	Binocular crowding ratio
Predictor	Bèta	Bèta	Bèta
Nystagmus amplitude	0.539**	0.206	0.347
Nystagmus frequency	-0.117	0.411	0.222
Strabismus	0.499*	-0.129	0.004
Astigmatism	0.048	-0.009	-0.246
Anisometropia	-0.065	0.408	0.322
Total $R^2$	0.549*	0.267	0.273

Note. \*  $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ .

**Table 6.5** Correlation matrix of predictors and crowding ratios separately for both patient groups (Alb.=Albinism, INS=Infantile Nystagmus Syndrome, CR=crowding ratio).

INS \ Alb.	Nystagmus amplitude	Nystagmus frequency	Strabismus	Astigmatism	Anisometropia	CR poorer eye	CR better eye	CR bino
Nystagmus amplitude		-0.48	-0.83**	0.68*	-0.09	-0.26	-0.36	-0.00
Nystagmus frequency	-0.02		0.39	-0.35	-0.08	0.54	0.56	0.63*
Strabismus	0.30	-0.11		-0.60*	-0.05	-0.26	0.08	-0.17
Astigmatism	-0.23	-0.14	-0.32		0.15	0.08	-0.47	-0.30
Anisometropia	-0.10	-0.23	0.11	0.01		-0.15	-0.02	-0.24
CR poorer eye	0.69**	-0.13	0.67**	-0.27	0.07		0.49	0.56*
CR better eye	0.24	0.20	-0.17	0.09	0.37	0.31		0.65*
CR bino	0.35	0.18	0.14	-0.38	0.23	0.44*	0.70**	

Note. \*  $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$  (one tailed  $p$ -test).

## **DISCUSSION**

The goal of this study was to compare mono- and binocular development in children with albinism, INS, and NV. Three hypotheses were evaluated: [1] interocular acuity differences will be larger in children with albinism and INS than in children with NV, [2] crowding ratios will be significantly higher in the poorer eye of children with albinism and INS than in children with NV, and [3] children with NV will show higher binocular summation ratios than children with albinism or INS.

### **Interocular differences**

Our first hypothesis was confirmed. Interocular acuity differences were larger in children with albinism and INS than in children with NV. For single and uncrowded acuity, interocular acuity differences were larger for both children with albinism and children with INS than for children with NV. In total, 6 children with albinism (37.5%) and 2 children with INS (20%) showed interocular acuity differences of 2 or more LogMAR lines on the crowded chart, which can be seen as an indicator of the presence of amblyopia (Dobson, et al., 2008). The lack of a group difference for the interocular differences measured with the crowded chart is probably caused by the nystagmus experienced by children with albinism and INS. As can be seen in the regression analysis, the monocular crowding ratio in the poorer eye and the better eye are both positively related with nystagmus characteristics. When a child has nystagmus, both eyes show fixational instability during monocular viewing and this might explain the lower acuities of both eyes when measured with a crowded chart.

### **Crowding ratios**

Our second hypothesis was partially confirmed. Children with albinism and INS had a higher binocular crowding ratio and poorer eye crowding ratio than children with NV. Children with INS also showed a higher crowding ratio in their better eye than children with NV. This probably has to do with the fact that nystagmus, or very unstable fixation, on its own causes larger contour interaction areas (Bedell & Loshin, 1991; Chung & Bedell, 1995; Simmers, et al., 1999). When looking at the magnitude of the crowding effect (amount of loss in acuity: Flom, 1991) in the poorer eye, crowding caused an acuity decrease of 2 LogMAR lines for children with albinism and INS and 1 LogMAR line for children with NV. The magnitude of the crowding effect in the better eye was still 2 LogMAR lines for children with INS and 1 LogMAR line for children with NV. These findings confirm the disturbing effect of retinal image motion and short fixation periods on crowded object recognition, even in the better eye.

As reported recently, visually impaired children (especially those with nystagmus) show higher binocular crowding ratios than children with NV when measured with

the C-test (Huurneman, Boonstra, Cillessen, et al., 2012). However, this study included 58 children with more than 10 different clinical diagnoses. The present sample consisted of 16 children with albinism and 10 with INS. Nystagmus occurs in both groups, and it is a frequently reported finding that nystagmus causes greater contour interaction and stronger foveal crowding effects (Chung & Bedell, 1995; Huurneman, Boonstra, Cox, et al., 2012). Interestingly, there are differences between idiopathic nystagmus and nystagmus in children with albinism (Kumar et al., 2011). Eye movement recordings collected in a study by Kumar et al. (2011) showed that nystagmus frequency was significantly lower in the group with albinism (mean 3.3 Hz) than the frequency observed for the idiopathic nystagmus group (mean 4.3Hz) and foveation characteristics (the subjects' ability to maintain fixation) were slightly better for the group with albinism. Finally, the study by Kumar et al. (2011) reported that strabismus and anomalous head posture were observed more frequently in the group with albinism, and stereopsis was worse compared with the idiopathic group. Therefore, it is not surprising that the binocular crowding ratios are higher in children with albinism and children with INS than in NV children. Monocular crowding ratios have not been reported before in these populations and reveal some remarkable findings about the higher prevalence of crowding in children with albinism and consistently higher crowding ratios in children with INS (regardless of viewing condition).

The strong crowding effects and large interocular acuity differences might influence reading performance (Huurneman, Boonstra, Cox, et al., 2012). Reading rates are slower in children and adults with albinism (Merrill, et al., 2011), adults with INS (only at near; Thomas, et al., 2011), and adults with strabismus (Kanonidou, Proudlock, & Gottlob, 2010). In 63 individuals with albinism, a large difference was found between reading acuity, i.e. the smallest print size a patient can resolve (0.53 LogMAR) and critical print size, i.e. the smallest print a patient can read with maximum reading speed (0.84 LogMAR) (Merrill, et al., 2011). Another recently published study has found equivalent information for individuals with INS with font sizes for optimal reading speed up to 6 LogMAR lines worse than NVA (Barot, et al., 2013). Reading acuity for young adults with NV was -0.12 LogMAR and critical print size was 0.04 LogMAR (Subramanian & Pardhan, 2006). The large difference between reading acuity and critical print size in individuals with albinism and INS might be related to contour interaction effects, as contour interaction reduces visibility and is scale-variant (Danilova & Bondarko, 2007). However, larger print size causes slower reading rates (Legge et al., 2007). Thus, two approaches can be employed to reduce crowding effects. The first is providing print size far above threshold reading acuity or enlarging letter spacing (adjust material). The second is training reading skills at threshold size. These two approaches warrant future research. Especially because recent findings

show that individuals with INS are capable of adopting strategies that elevate reading speeds to rates much higher than expected on the basis of their oculomotor and foveal deficits (Thomas, et al., 2011).

### **Binocular summation ratios**

Our third hypothesis was not confirmed. The median binocular summation ratios did not differ between children with NV and children with albinism or INS, indicating similar development of the dominant eye and binocular acuity in the three groups. There was larger intragroup variability in children with albinism than in the other groups. Fifty percent (4 out of 8) of the children with 2 or more LogMAR lines interocular acuity differences showed binocular inhibition. Binocular inhibition has been reported in 9.5% of children with intermittent exotropia (Ahn, Yang, & Hwang, 2012), and in adults with anisometropic and strabismic amblyopia (Pardhan & Gilchrist, 1992). Two explanations are presented for a lack of group differences in binocular summation. The first reason for this might be that the present study used coarser scoring methods compared to scoring methods used in previous studies with smaller step sizes (Pardhan, 1993; Vedamurthy, et al., 2007). It is possible that more sensitive scoring leads to more differentiation. The second reason for a lack of group differences might be that the patient groups showed reduced nystagmus amplitudes for binocular viewing, leading to higher binocular visual acuities which could mask effects on binocular summation (i.e. lead to a higher binocular summation ratio or mask binocular inhibition). Future research should use more sensitive scoring methods and measure nystagmus amplitudes under mono- and binocular viewing conditions.

Monocular and binocular acuities have a different developmental time path. Vedamurthy et al. (2007) reported that visual acuity in the dominant eye still increased in children with NV aged 6-14 years ( $r = -0.5$ ) while binocular acuity did not ( $r = -0.2$ ). In our study, dominant eye crowded acuity and binocular crowded acuity in children with NV and albinism both strongly improved with age (both acuities  $r > -0.7$ ). The correlation was slightly weaker in children with INS (crowded acuity better eye  $r = -0.5$  and binocular crowded acuity  $r = -0.2$ ), emphasizing that nystagmus is strongly associated with acuity (Simmers, et al., 1999).

Single acuity measured in the dominant eye of children with NV improved more with age than binocular single acuity ( $r$ 's =  $-0.5$  and  $-0.3$ , respectively). In children with albinism or INS, both dominant eye and binocular single acuity still increased with age (range of  $r$   $-0.6$  to  $-0.7$ ). Thus, crowded acuities developed similarly with age in children with NV and children with albinism, but single acuity seemed to mature earlier in children with NV than in children with albinism and INS, which might indicate slower maturation of the visual system.

**Predictors of crowding**

Strabismus and nystagmus amplitude both significantly predicted crowding in the poorer eye. A separate analysis for each patient group showed that only the crowding ratio in the poorer eye of children with albinism could be predicted by the presence of strabismus and the nystagmus amplitude. The crowding ratio in the poorer eye of children with INS could not be significantly predicted by nystagmus frequency and strabismus. Anisometropia and astigmatism did not predict the height of the crowding ratio in the poorer eye. These findings are in line with studies revealing that the presence of strabismus predicts stronger crowding effects (Bonneh, Sagi, & Polat, 2004; Greenwood, et al., 2012). Recent research has investigated interocular acuity differences and crowding in three groups: 4-9 year old children with strabismus, children with anisometropic amblyopia, or mixed strabismus/anisometropia (Greenwood, et al., 2012). Significant interocular acuity differences occurred in all three clinical groups, but only the strabismic and mixed group showed significant crowding. In anisometropia, crowding effects are found to be normal, that is, scale with the size of the pattern, but this does not hold for strabismic amblyopes (Bonneh, et al., 2004; Greenwood, et al., 2012).

The crowding ratio in the better eye and the binocular crowding ratio were not significantly predicted by our five variables, neither were they in the separate patient group analysis. Nystagmus frequency and anisometropia were marginally significant predictors of the crowding ratio in the better eye. The shorter foveation times, or greater retinal slip, tended to predict higher crowding ratios in the better eye. This is in line with earlier findings (Pascal & Abadi, 1995; Simmers, et al., 1999). The amount of anisometropia had a marginally significant influence on the crowding ratio in the better eye. However, only 5 of the children with albinism or INS had interocular differences > 1 dioptre in spherical refraction. Only one child had more than 1 dioptre interocular differences in cylindrical refraction. This might explain the lack of correlation of this variable with our dependent measures (restricted range). Future research would be necessary to provide more insight into the contribution of anisometropia on monocular crowding ratios. The strongest predictor of the binocular crowding ratio was the nystagmus amplitude, but this predictor was not statistically significant. Of course, it should be mentioned that a weakness of this study is its sample size for a regression with five predictors. An explanation for a lack of significant predictors for the binocular crowding ratio is that the influence of attentional mechanisms is not considered, while these factors are also mentioned as an explanation for the strength of crowding especially in children (Huurneman, Boonstra, Cox, et al., 2012).

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**Supplement.** *Clinical characteristics of visually impaired children.*

A. Children with albinism										
ID	Sex	Age	DVAc* poorer eye	DVAc better eye	Deviation	Stereopsis (sec arc)	Nystagmus frequency (Hz)	Nystagmus amplitude (degrees)	Treatment	Correction
101	M	7	0.80	0.80	orthophoria	100	7	7	n.a.	R S:+0.75 C:-5.00 L S:+0.75 C:-4.50
114	F	8	1.00	0.70	R esotropia	nil	3.5	5	Surgery	R S:+7.25 C:-4.25 L S:+7.00 C:-3.75
116	F	6	1.30	1.00	R esotropia	nil	4	3	Patching	No correction
117	M	6	1.30	1.30	orthophoria	No measurements.	3	6	n.a.	R S:+4.75 C:-2.50 L S:+4.50 C:-3.75
119	M	7	0.80	0.80	R esotropia	nil	4	2.5	Surgery	R S:+2.00 C: plan L S:+2.00 C: plan
121	M	7	0.80	0.40	orthophoria	nil	0**	0**	n.a.	No correction
127	M	7	0.50	0.40	orthophoria	400	0**	0**	n.a.	R S:-+1.50 C:-2.00 L S:+1.25 C:-1.25
130	M	5	0.80	0.80	orthophoria	400	2	8	n.a.	R S:-0.25 C:-1.00 L S: plan C:-1.75
134	M	5	1.10	0.80	L esotropia	nil	2	14.5	Patching	R S: plan C:-1.75 L S: plan C:-1.00
138	F	5	1.00	0.90	orthophoria	nil	5	2.5	n.a.	R S:+1.00 C:-2.00 L S:+2.50 C:-2.25
144	M	4	1.50	1.50	orthophoria	nil	3	12.5	n.a.	R S:+3.50 C:-2.75 L S:+5.00 C:-2.00
145	M	4	1.50	1.50	R exotropia	100	3	12.5	Patching	R S:+6.00 C:-2.50 L S:+3.75 C:-2.50
150	M	4	1.40	1.10	R exotropia	nil	2	9	No treatment	R S:+4.25 C:-2.00 L S:+4.75 C:-2.00
159	M	8	0.70	0.60	orthophoria	800	4	7	n.a.	R S:+4.50 C:-3.25





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Perceptual learning in  
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**ABSTRACT**

**Purpose:** This study investigated whether visual perceptual learning can improve near visual acuity and reduce foveal crowding effects in four-to nine-year-old children with visual impairment.

**Methods:** Participants were 45 children with visual impairment and 29 children with normal vision. Children with visual impairment were divided into three groups: a magnifier group ( $n = 12$ ), a crowded perceptual learning group ( $n = 18$ ), and an uncrowded perceptual learning group ( $n = 15$ ). Children with normal vision were also divided in three groups, but were only measured at baseline. Dependent variables were: single near visual acuity (NVA), crowded NVA, LH line 50% crowding NVA, number of trials, accuracy, performance time, amount of small errors and amount of large errors. Children with visual impairment trained during 6 weeks, 2 times per week, for 30 minutes (12 training sessions).

**Results:** After training, children showed significant improvement of NVA in addition to specific improvements on the training task. The crowded perceptual learning group showed the largest acuity improvements (1.7 LogMAR lines on the crowded chart,  $p < 0.001$ ). Only the children in the crowded perceptual learning group showed improvements on all NVA charts.

**Conclusions:** Children with visual impairment benefit from perceptual training. While task specific improvements were observed in all training groups, transfer to crowded NVA was largest in the crowded perceptual learning group. To our knowledge, this is the first study to provide evidence for the improvement of NVA by perceptual learning in children with visual impairment.

## INTRODUCTION

Perceptual learning (PL) is considered to be any relatively permanent and consistent change in the perception of a stimulus array, following practice or experience with this array (Gibson, 1963; Green & Bavelier, 2007). The first evidence that perceptual abilities can be improved by practice go back to the middle of the 19<sup>th</sup> century (Volkman, 1858). PL can improve a range of visual functions: spatial resolution (Green & Bavelier, 2007), stereo acuity (Astle, McGraw, & Webb, 2011), orientation discrimination (Jehee, Ling, Swisher, van Bergen, & Tong, 2012; Schiltz et al., 1999), motion direction (Thompson, Tjan, & Liu, 2013), contrast sensitivity (Polat, Ma-Naim, & Spierer, 2009), texture perception (Hussain, Bennett, & Sekuler, 2012), and depth perception (Uka, Sasaki, & Kumano, 2012). From a neuroscience perspective, it has been suggested that PL illustrates the remarkable capacity of early sensory cortex plasticity (Gilbert, Li, & Piech, 2009). However, training effects can also transfer to untrained locations and orientations, suggesting a rule-based learning model in which higher-order processing areas learn the rules of reweighting V1 inputs through training (Doshier & Lu, 1998). Attention, mediated by higher-level visual areas, is thought to determine which representations in lower-level areas undergo plasticity and gates learning (Baker, Olson, & Behrmann, 2004). There are three general principles of PL for clinical application: [1] practice needs to occur under conditions where performance is severely impaired with trial by trial feedback, [2] a stopping rule needs to be incorporated (at plateau performance), and [3] stimuli and tasks need to be interesting and engaging (Levi & Li, 2009). Finally, accurate refractive correction is essential before the commencement of PL, and the refraction should be regularly reviewed and refined during training (Levi & Li, 2009; Sunness & El Annan, 2010).

PL techniques have been evaluated in different patient populations: amblyopia (Levi & Li, 2009; Polat, et al., 2009), age-related macula degeneration (visual search : Liu, et al., 2007, reading speed: Chung, 2011; Yu, Cheung, Legge, & Chung, 2010; Yu, Legge, Park, Gage, & Chung, 2010), visuospatial disorders after stroke (line orientation discrimination: Funk et al., 2013), bilateral cortical blindness (visual field stimulation : Stoerig, 2008; Trevethan, Urquhart, Ward, Gentleman, & Sahraie, 2012), schizophrenia (motion perception: Norton, McBain, Ongur, & Chen, 2011), low myopia and early presbyopia (visual acuity: Durrie & McMinn, 2007), patients with hippocampal damage (face recognition: Graham et al., 2006), and Parkinson's disease (artificial grammar and category learning: Reber & Squire, 1999).

PL has not yet been applied as a rehabilitation method for children with visual impairment (VI) (Huurneman, Boonstra, Cox, et al., 2012). A visual impairment during childhood obviously causes impoverished visual acuity and/or reduced contrast sensitivity. Recent research indicates that abnormal lower level visual

processing influences mid-to-high level visual processes, such as visual search speed and accuracy (Liu, et al., 2007; MacKeben & Fletcher, 2011; Tadin, et al., 2012), peripheral crowding and motion processing (Huurneman, Boonstra, Cillessen, et al., 2012; Tadin, et al., 2012), and foveal crowding effects (Huurneman, Boonstra, Cillessen, et al., 2012). Explanations for slower visual search in children with VI are reduced foveal acuity and the demands for attentional resources to attend to foveal information and reduced attention for peripheral stimuli (Tadin, et al., 2012), or visuo-attentional impairments (Cavezian et al., 2012). Little is known about rehabilitation outcomes in children with VI (Binns et al., 2012). To fill this gap, the present study examined whether the development of (crowded) near visual acuity (NVA) can be stimulated and whether crowding effects can be reduced by PL, which seems to be an effective method to reduce foveal crowding in subjects with amblyopia (Huurneman, Boonstra, Cox, et al., 2012).

Three interventions were compared: [1] a magnifier task in which children searched for a unique optotype in a row with distracters (experimental/crowded task), [2] a PL task where crowding effects were evoked (experimental/crowded task; PLc), and [3] a PL task in which optotypes were separated at such a distance that no contour interaction occurred (control/uncrowded task; PLu). Based on previous research by our group (Cox, et al., 2009; Huurneman, Boonstra, Cillessen, et al., 2012; Huurneman, Boonstra, Cox, et al., 2012), and by others, four hypotheses were formulated: [1] children with VI have higher crowding ratios and poorer baseline performance on the training task than children with normal vision (NV), [2] the PLc task is most effective in reducing crowding effects and improving NVA, [3] task specific learning effects and transfer to untrained visual functions, such as NVA, occur in all training groups, and [4] improvements are larger for 7-9 year-old children than 4-6 year-old children, because focused attention is weaker in young children and functions as a gateway to ensure that PL occurs only in response to features to which attention is directed.

## **METHODS**

### **Participants**

Participants were 45 children with VI and 29 children with NV. Inclusion criteria for both groups were: age between 4 and 9 years and normal developmental level. Inclusion criteria for children with VI were: distance visual acuity (DVA) between 20/400 and 20/40, normal birth weight (at least 3000 gr), birth at term (at least 36 weeks), no perinatal complications, no additional impairments, and intact visual field. The Table presents the average age and DVA of the children with VI and with NV. Supplement A presents clinical diagnosis and characteristics of all children with VI. Informed consent was obtained from the parents of all children after explanation of



**Table** *Average characteristics of children with NV and VI. Age is presented in months and DVA is presented in LogMAR notation for the crowded version of the C-test. Children with NV were not trained, but were measured with the training material at baseline. M, magnifier group.*

	NV						VI					
	4-6y			7-9y			4-6y			7-9y		
	M <sup>†</sup>	PLc <sup>†</sup>	PLu <sup>‡</sup>	M	PLc	PLu	M	PLc	PLu	M	PLc	PLu
<b>N</b>	5	6	4	4	4	6	7	11	7	5	7	8
<b>Age</b>	64.2 (6.7)	71.2 (10.8)	68.0 (12.7)	96.0 (8.0)	97.3 (7.9)	94.5 (8.7)	69.9 (6.8)	68.5 (6.4)	67.0 (9.6)	91.4 (3.6)	102.0 (8.3)	99.5 (7.9)
<b>DVA</b>	0.14 (0.16)	0.05 (0.11)	0.02 (0.10)	-0.08 (0.05)	-0.08 (0.05)	-0.07 (0.05)	0.84 (0.18)	0.80 (0.23)	0.70 (0.37)	0.66 (0.13)	0.66 (0.30)	0.63 (0.18)

the nature and possible consequences of the study. The local ethics committee approved the study before the assessments were conducted (CMO Arnhem-Nijmegen). The study was conducted in accordance with the Declaration of Helsinki (1969).

### Ophthalmological examination

All children participated in an ophthalmological exam before the start of the experiment. Visual acuity was measured mono- and binocularly on 5 m with the C-test (Haase & Hohmann, 1982; Hohmann & Haase, 1993) and at 6 m binocularly with the tumbling E-chart (Taylor, 1978) under controlled lighting conditions. NVA was determined binocularly with the LH-version of the C-test (Huurneman, Boonstra, Cillessen, et al., 2012) and the LH line 50% crowding chart (Hyvarinen, et al., 1980) at 40 cm (distance was carefully monitored with a ruler). The LH-version of the C-test contains two chart versions with absolute spacing (Huurneman, Boonstra, Cillessen, et al., 2012). The crowded chart had an interoptotype spacing of 2.6', and the single chart had an interoptotype spacing of  $\geq 30'$  at 40 cm. The LH line 50% crowding chart contains interoptotype spacing that is 50% of the size of the optotype (therefore 50% crowding chart). Children were asked to identify the first five symbols in a row, which were pointed out with a pencil, and could progress to the next line if they correctly identified 3 or more out of the 5 symbols. If there were fewer than 5 symbols in a row, children could progress if they could correctly identify at least half of the symbols.

A gross estimation of the visual field was obtained by confrontational techniques. In case of retinal disease children were tested on central or peripheral scotomas with dynamic perimetry (Goldmann). Of the 10 children with retinal diseases, 9 had an intact visual field and 1 6-year old girl with retinal dystrophy had a small concentric limitation of the left eye. No central scotomas were found and therefore we decided to

include her in the study. Objective refraction was obtained after cycloplegia and if necessary spectacle correction was prescribed or changed before the experiment and training period started.

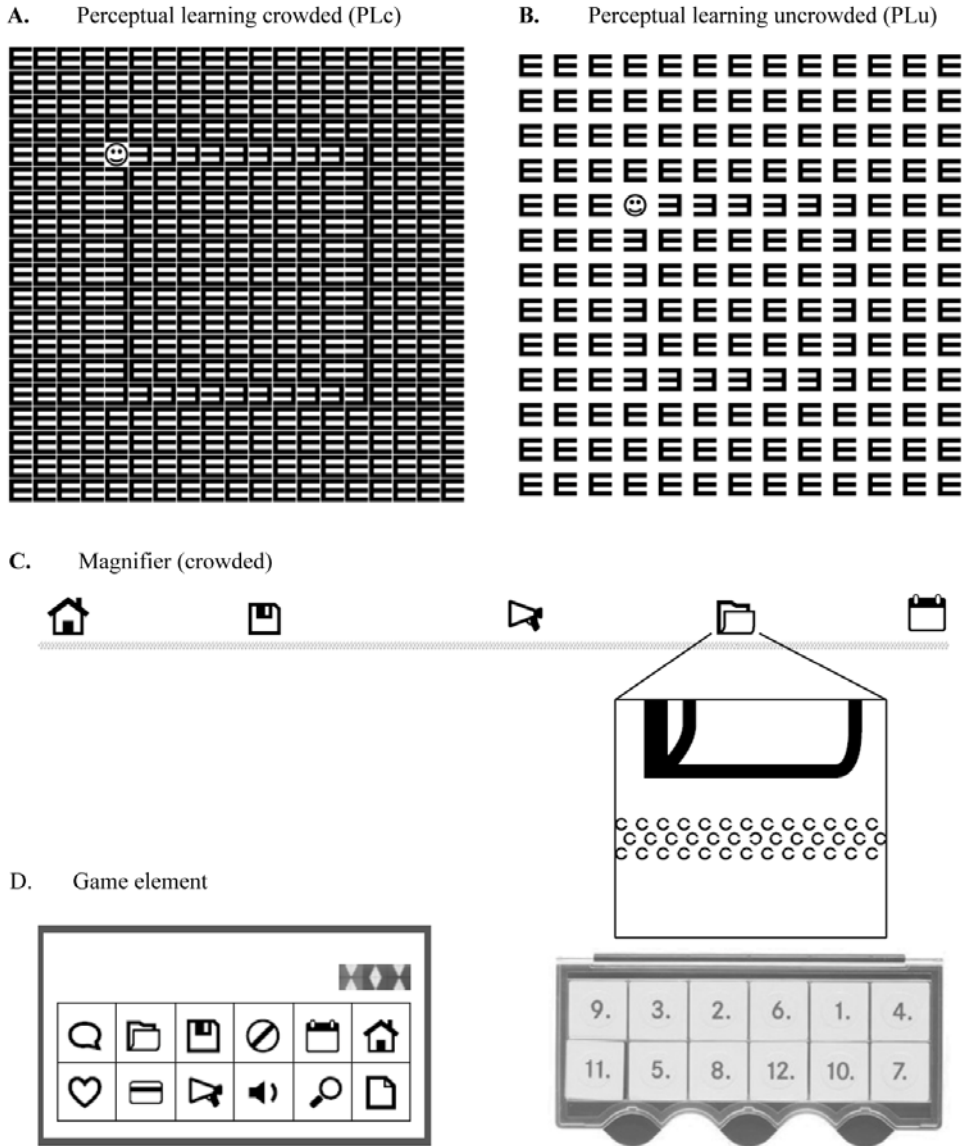
### **Training paradigms**

Two experimental training paradigms and one control training were developed. The training paradigms were inspired by the Eriksen flanker task (Eriksen, 1974). The training groups were matched with respect to age and DVA (see Table).

The first experimental training was a visual search training in which the child had to follow the trail of inversed E's in a 145 mm x 145 mm grid (see Figure 7.1A). At baseline, this grid consisted of symbols of 7.0 mm. Edge-to-edge optotype spacing was fixed at 0.3 mm ( $0.04^\circ$  at 40 cm; consistent with spacing of the crowded chart of the C-test). A smiley was placed at the beginning of the trail. In order to make the training easier for the children, we let the children draw the trail. The children had to start and end at the smiley, and by doing this they drew a figure. All children started working with optotypes sized 4 M (1.0 LogMAR at 40 cm/ 7.0 mm) at the first training session and could progress to 2 M (0.5 LogMAR at 40 cm/ 3.5 mm) and subsequently 1 M (0.25 LogMAR at 40 cm/ 1.75 mm) if they could draw a figure without making errors and could complete 12 trials in a 30 minute training session (see Supplement B). The control training consisted of exactly the same game, but with a fixed edge-to-edge spacing of 3.6 mm ( $0.52^\circ$  at 40 cm; consistent with spacing of the single chart of the C-test; see Figure 7.1B). On average, children started to work with 2M optotypes after 3 weeks and with 1M optotypes after 4 weeks of training (progress was the same for the PLc and PLu training groups).

The second experimental training paradigm was a crowded magnifier training. This training was developed, because recent studies have demonstrated that children profit from a magnifier training (Boonstra et al., 2012). The magnifier group trained with different material due to practical issues that disabled us to use the same design as the PL groups; (i) the stimulus would be highly unattractive, (ii) children could not draw a line while using the magnifier. We created a 191 mm array containing three rows with Landolt C's sized 0.32 M (-0.1 LogMAR at 40 cm/ 0.5 mm) with an edge-to-edge element spacing of 0.3 mm. Children had to search for the inversed Landolt C in this row with an electronic handheld magnifier with a display size of 3.5", providing  $8 \times$  magnification (see Figure 7.1C).

A game element was incorporated for each of these training paradigms to provide feedback and to make the training engaging. Each training session consisted of 12 trials. Answer options were combined with tiles that the child could place on one of 12 answer boxes. If all tiles were placed correctly, they formed a pattern matching the pattern in the upper right corner of the page (see Figure 7.1D). During the training



**Figure 7.1** (A) An example of a stimulus used for the PLc training. The child must search (B) Represents the uncrowded version of this task (serving as a control task by not inducing contour interaction). (C) Presents an example of stimulus in the magnifier task. The child must search for the inversed C in a crowded search strip and uses an electronic magnifier while searching for the inversed optotype. (D) Presents an example of the game element. The correct answer is the paper map.

pre-test and post-test performance of children with VI was measured with a repeated measures ANOVA. Age category and training group were the independent variables.

sessions, children could adopt a self-chosen distance.

### **Procedure**

At baseline, NVA and performance on the training task were measured. Children with NV were seen once as a reference group at baseline. For children with VI, this baseline performance counted as their pre-test score. Training started within 2 weeks after the pre-test. During the training period, children with VI were seen 2× a week for a period of 6 weeks (12 training sessions). Each training session consisted of 30 minutes of practice on the training task. Trainers visited children at their schools. Within two weeks after the last training session children performed the post-test. The post-test measurement consisted of the same measures as the pre-test.

### **Statistical Analysis**

There were 7 main outcome measures. With regards to visual functions: [1] binocular NVA with the LH-version of the C-test (single and crowded NVA) and the LH line 50% crowding chart, and [2] the crowding ratio (single NVA/crowded NVA) (Huurneman, Boonstra, Cillessen, et al., 2012). Performance on the training task was of correct trials (tiles placed correctly/total number of trials), [3] performance time, and (only for the PL tasks): [4] number of small errors (incorrectly drawing 1 non-inversed E), and [5] number of large errors (incorrectly drawing > 1 non-inversed E). First, baseline performance for crowding ratios and training task measures were compared between children with NV and children with VI with a univariate ANOVA. Age category (4-6-years vs. 7-9-years), group (NV or VI), and training group (magnifier, PLc, and PLu) were the independent variables. The differences between Separate post-hoc ANOVAs were run using Bonferroni statistics to disentangle interaction effects (significance level  $\alpha = 0.05$ ).

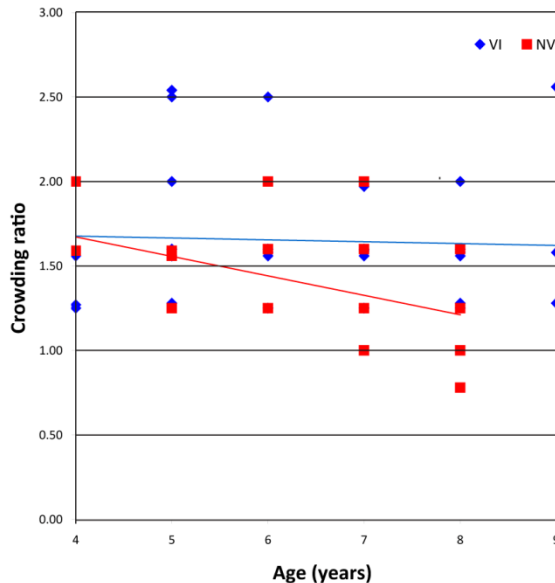
## **RESULTS**

### **Group Differences at Baseline**

There were 6 children with VI and 1 child with NV that were unable to perform the training task at baseline. As a result we had a smaller sample size for 4 training task measures: accuracy, performance time, and small and large errors for these children.

**Crowding ratio.** Children with NV had a lower crowding ratio (1.42) than children with VI (1.66),  $F(1, 62) = 7.81$ ,  $p = 0.007$ , partial  $\eta^2 = .11$  (see Figure 7.2). Age categories and training groups did not differ ( $p$ 's > 0.07). No interaction effects were found.

**Number of trials.** There were no group or training group differences ( $p$ 's > 0.07). Age categories differed in the number of trials: 4-6 year olds executed less trials (7.1) than 7-9 year olds (11.8),  $F(1, 62) = 33.68$ ,  $p < 0.001$ ,  $\eta^2 = .35$ . No interaction effects were



**Figure 7.2** Crowding ratios for the children with normal vision (NV) and the children with visual impairment (VI) as a function of age. Children with VI show higher crowding ratios than children with NV at baseline.

found.

**Accuracy.** There were no group differences in accuracy,  $F(1, 55) = 0.29$ ,  $p = 0.595$ , partial  $\eta^2 = .01$ . Age categories differed: 4-6 year old children were less accurate (76.4%) than 7-9 year old children (90.6%),  $F(1, 55) = 6.19$ ,  $p = 0.016$ , partial  $\eta^2 = .10$ . Training groups also differed: children were more accurate in the magnifier group (98.3%) than in the PLc and PLu group (resp. 74.7% and 77.6%),  $F(2, 55) = 6.37$ ,  $p = 0.003$ , partial  $\eta^2 = .19$ . No interaction effects were found.

**Performance time.** There were no differences between the NV and VI group or training group differences ( $p$ 's  $> 0.27$ ). Age categories differed: 4-6 year olds were slower (72.1 s) than and 7-9 year olds (52.6 s),  $F(1, 55) = 7.32$ ,  $p = 0.009$ ,  $\eta^2 = .12$ . No interaction effects were found.

**Small errors.** Groups, age categories, and training groups did not differ ( $p$ 's  $> 0.55$ ). No interaction effects were found.

**Large errors.** Groups differed: children with VI made more large errors (0.66) than children with NV (0.28 errors),  $F(1, 39) = 5.26$ ,  $p = 0.027$ , partial  $\eta^2 = .12$ . Age categories and training groups did not differ ( $p$ 's  $> 0.37$ ). No interaction effects were found.

### Crowding Training: Children with Visual Impairment

Preliminary linear regression analysis showed that the improvement in single and

crowded NVA after training could not be predicted by the child characteristics age (months), single NVA at baseline, sex, or pathology (retinal, iris, nystagmus, or lens), respectively,  $F(4, 40) = 0.08, p = 0.989$ , and  $F(4, 40) = 0.99, p = 0.425$ . There was no difference in NVA improvement between children with and without nystagmus (single NVA;  $p=0.91$ : crowded NVA ;  $p=0.57$ : LH line 50% crowding;  $p=0.34$ : crowding ratio;  $p=0.60$ ).

**Single NVA.** Children showed improved single NVA after training,  $F(1, 39) = 31.43, p < 0.001$ , partial  $\eta^2 = .45$  (see Figure 7.3A). Average acuity was 0.54 LogMAR ( $SE = 0.04$ ) at pre-test and 0.41 LogMAR ( $SE = 0.05$ ) at post-test. Training groups showed no difference in the amount of improvement,  $F(2, 39) = 0.63, p = 0.536$ , partial  $\eta^2 = .03$ , nor did age categories,  $F(1, 39) = 0.38, p = 0.539$ , partial  $\eta^2 = .01$ . Thus, single NVA improved for both age categories and all training groups. No interaction effects were found.

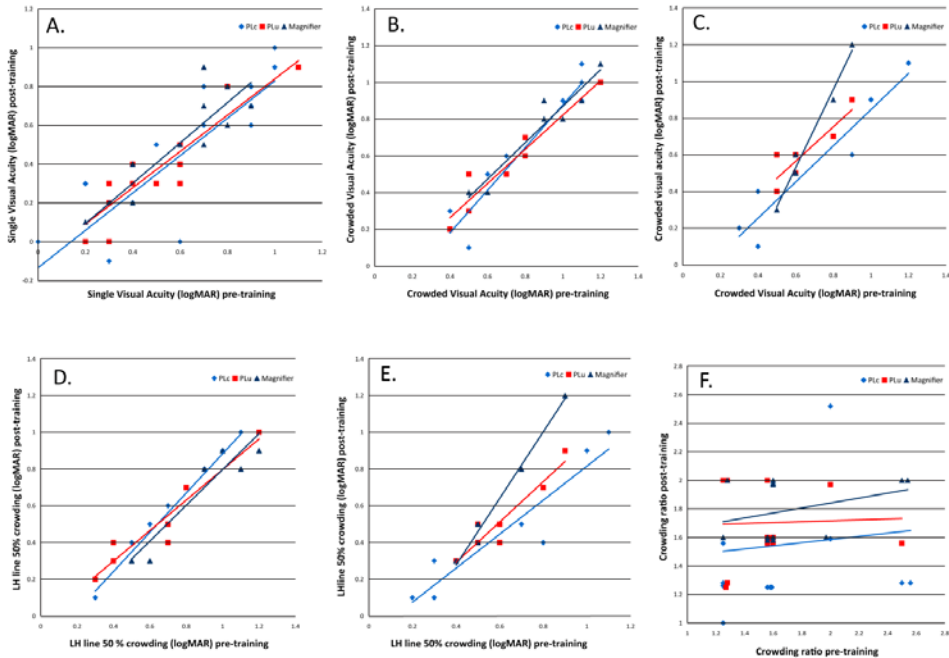
**Crowded NVA.** There was a pre-post  $\times$  training group interaction effect,  $F(2, 39) = 3.93, p = 0.028$ , partial  $\eta^2 = .17$ . In the magnifier group, crowded NVA did not improve,  $F(1, 10) = 1.89, p = 0.200$ , partial  $\eta^2 = .16$ . There was no pre-post  $\times$  age interaction,  $F(1, 10) = 3.53, p = 0.090$ , partial  $\eta^2 = .26$ . Crowded NVA did not improve for children in the magnifier group (see Figure 7.3B-C).

In the PLc group, there was an improvement of crowded NVA in both age categories,  $F(1, 16) = 33.60, p < 0.001$ , partial  $\eta^2 = .68$ . Crowded NVA was 0.76 LogMAR ( $SE = 0.07$ ) at pre-test and 0.59 LogMAR at post-test ( $SE = 0.08$ ). There was no pre-post  $\times$  age interaction,  $F(1, 16) = 0.28, p = 0.603$ , partial  $\eta^2 = .02$  (see Figure 7.3B-C).

In the PLu group, there was a pre-post  $\times$  age interaction,  $F(1, 13) = 9.15, p = 0.010$ , partial  $\eta^2 = .41$ . For the 4-6 year old children, crowded NVA improved,  $F(1, 6) = 27.92, p = 0.002$ , partial  $\eta^2 = .82$  (see Figure 3B). Crowded NVA was 0.70 LogMAR ( $SE = 0.10$ ) at pre-test and 0.54 LogMAR ( $SE = 0.10$ ) at the post-test. For the 7-9 year olds, crowded NVA did not improve,  $F(1, 7) = 2.03, p = 0.197$ , partial  $\eta^2 = .23$  (see Figure 7.3C).

Thus, the PLc group was the only training group that showed a significant improvement in crowded NVA for both age categories. The magnifier group showed no progress in crowded NVA and only the 4-6 year olds in the PLu group showed improved crowded NVA.

**LH line 50% crowding.** There was a three-way pre-post  $\times$  age category  $\times$  training interaction,  $F(2, 39) = 5.85, p = 0.006$ , partial  $\eta^2 = .23$ . In the magnifier group, there was a pre-post  $\times$  age interaction,  $F(1, 10) = 9.77, p = 0.011$ , partial  $\eta^2 = .49$ . The LH line 50% crowding NVA of 4-6 year olds improved,  $F(1, 6) = 28.00, p = 0.002$ , partial  $\eta^2 = .82$  (see Figure 7.3D). LH line 50% crowding NVA was 0.89 LogMAR at pre-test and 0.69 LogMAR at post-test. The 7-9 year-olds showed no improvement,  $F(1, 4) = 0.286, p = 0.621$ , partial  $\eta^2 = .07$  (see Figure 3E), indicating an age specific effect of



**Figure 7.3** (A) Presents the single NVA chart pre- and post-training. (B) Pre- and post-training crowded NVA for four-to-six year olds. (C) Pre- and post-training crowded NVA for the seven-to-nine year olds. (D) Pre- and post-training LH line 50% crowding NVA for the four-to-six year olds. (E) Pre- and post-training LH line 50% crowding NVA for the seven-to-nine year olds. (F) The crowding ratios pre- and post-training.

the magnifier training.

In the PLc group, LH line 50% crowding NVA improved,  $F(1, 16) = 41.35$ ,  $p < 0.001$ , partial  $\eta^2 = .72$ . LH line 50% crowding NVA was 0.67 LogMAR ( $SE = 0.07$ ) at pre-test and 0.53 LogMAR ( $SE = 0.07$ ) at post-test. There was no pre-test  $\times$  age interaction,  $F(1, 16) = 0.21$ ,  $p = 0.655$ , partial  $\eta^2 = .01$  (see Figure 7.3D-E). Similar to the crowded NVA, both age categories benefitted from the PLc training.

In the PLu group, LH line 50% crowding NVA also improved,  $F(1, 13) = 29.98$ ,  $p < 0.001$ , partial  $\eta^2 = .70$ . There was no pre-test  $\times$  age interaction,  $F(1, 13) = 1.73$ ,  $p = 0.211$ , partial  $\eta^2 = .12$ . LH line 50% crowding NVA was 0.63 LogMAR ( $SE = 0.06$ ) at pre-test and 0.51 LogMAR ( $SE = 0.06$ ) at post-test (see Figure 7.3D-E). LH line 50% crowding NVA improved for both age categories. The two PL groups showed improved LH line 50% crowding NVA for both age categories and the magnifier group showed improvements for the 4-6 year olds.

**Crowding ratio.** Crowding ratios did not change after training,  $F(1, 39) = 0.04$ ,  $p = 0.835$ , partial  $\eta^2 = .00$ . Training groups did not differ,  $F(2, 39) = 1.05$ ,  $p = 0.359$ , partial  $\eta^2 = .05$ , nor did age categories,  $F(1, 39) = 0.76$ ,  $p = 0.389$ , partial  $\eta^2 = .02$  (see

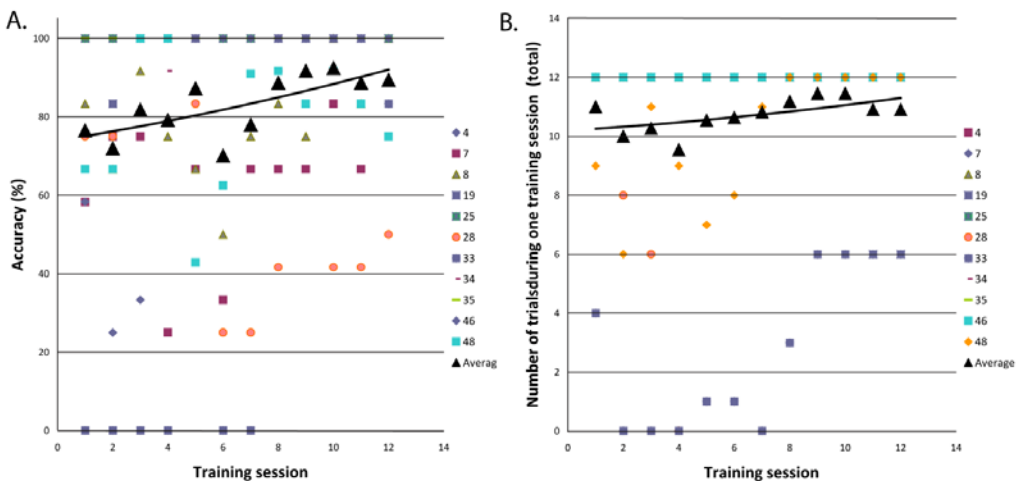
Figure 7.3F). No interaction effects were found. Although crowding ratios did not change at group level, 8 out of 18 children in the PLc group showed a reduction of the crowding ratio, 2 out of 12 children in the magnifier group, and only 1 out of 15 children in the PLu group. Thus, crowding ratios did not change after training.

**Performance on Training Task**

**Number of trials.** There was a pre-post  $\times$  age interaction,  $F(2, 39) = 25.66, p < 0.001$ , partial  $\eta^2 = .40$ . The 4-6 year olds completed more trials at post-test,  $F(1, 22) = 37.32, p < 0.001$ , partial  $\eta^2 = .63$ . Children completed 5.8 trials ( $SE = 1.00$ ) at pre-test and 11.7 ( $SE = 0.20$ ) at the post-test (for examples of progress during training see Figure 7.4A-B). There was no pre- post  $\times$  training interaction,  $F(2, 22) = 0.57, p = 0.571$ , partial  $\eta^2 = .05$ . All 4-6 year olds showed an increase of the number of trials performed. The 7-9 year-old children did not perform more trials during the post-test,  $F(1, 17) = 1.74, p = 0.204$ , partial  $\eta^2 = .09$ . Children completed 11.7 trials ( $SE = 0.2$ ) at pre-test and 12.0 trials ( $SE = 0.0$ ) at post-test. There was no pre-post  $\times$  training interaction,  $F(2, 17) = 0.61, p = 0.554$ , partial  $\eta^2 = .07$ . Thus, only the 4-6 year olds completed significantly more trials after training.

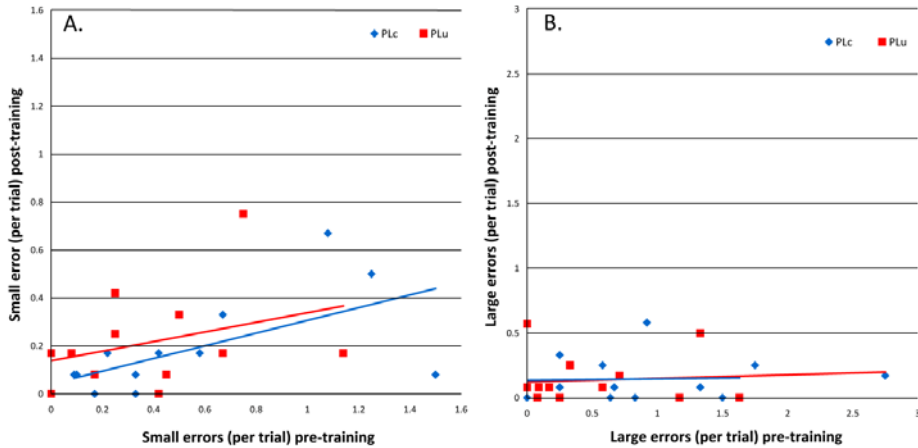
**Accuracy.** Accuracy improved after training,  $F(1, 33) = 15.60, p < 0.001$ , partial  $\eta^2 = .32$ . Accuracy at pre-test was 85.1% ( $SE = 3.4\%$ ) and 98.7% ( $SE = 0.7\%$ ) at post-test. There were no differences in amount of improvement between training groups,  $F(2, 33) = 2.40, p = 0.107$ , partial  $\eta^2 = .13$ , or between age groups,  $F(2, 33) = 2.50, p = 0.123$ , partial  $\eta^2 = .07$ . No interaction effects were found.

**Performance time.** Performance time decreased after training,  $F(1, 33) = 119.58, p < 0.001$ , partial  $\eta^2 = .78$ . Performance time was 65.2 s ( $SE = 4.7$  s) at pre-test and



**Figure 7.4** (A) Presents accuracy and (B) presents number of trials for four-to-six-year-old children in the PLc group as a function of training session.





**Figure 7.5** (A) Presents small errors and (B) presents large errors pre- and post-training.

17.9s ( $SE = 1.6$  s) at post-test. There was no difference between training groups,  $F(2, 33) = 0.13$ ,  $p = 0.878$ , partial  $\eta^2 = .01$ , or age  $F(1, 33) = 2.82$ ,  $p = 0.103$ , partial  $\eta^2 = .08$ . No interaction effects were found. All training groups showed a shorter performance time after training.

**Small errors.** Small errors decreased after training,  $F(1, 24) = 5.85$ ,  $p = 0.023$ , partial  $\eta^2 = .20$ . Children made 0.45 errors ( $SE = .08$ ) at pre-test and 0.25 errors ( $SE = .05$ ) at post-test (see Figure 7.5A). There was no difference between training groups,  $F(1, 24) = 0.06$ ,  $p = 0.812$ , partial  $\eta^2 = .00$ , or age categories,  $F(1, 24) = 0.02$ ,  $p = 0.894$ , partial  $\eta^2 = .00$ . No interaction effects were found. All training groups showed a decrease of small errors after training.

**Large errors.** Large errors also decreased after training,  $F(1, 24) = 14.22$ ,  $p = 0.001$ , partial  $\eta^2 = .37$ . Children made 0.66 ( $SE = 0.13$ ) large errors at pre-test and 0.16 ( $SE = 0.03$ ) errors at post-test (see Figure 7.5B). There was no difference between training groups,  $F(1, 24) = 0.86$ ,  $p = 0.362$ , partial  $\eta^2 = .04$ , or age categories,  $F(1, 24) = 1.43$ ,  $p = 0.243$ , partial  $\eta^2 = .06$ . No interaction effects were found. As for the number of small errors, all training groups showed a decrease of large errors after training.

## DISCUSSION

This study compared the effectiveness of three training paradigms to reduce crowding effects and improve NVA in children with VI. Four hypotheses were evaluated: [1] children with VI show a higher crowding ratio and poorer baseline performance on the training task than children with NV, [2] the experimental PL task is most effective in reducing crowding effects and improving NVA, [3] task specific learning effects and transfer to untrained visual functions such as NVA occur in all training groups (generalization of learning effect), and [4] improvements are larger for 7-9 year old

children than 4-6 year old children.

### **Baseline Group Differences**

Our first hypothesis was confirmed. Children with VI showed a higher baseline crowding ratio than children with NV. This replicates our earlier study with comparable children (Huurneman, Boonstra, Cillessen, et al., 2012). The children with VI also showed poorer performance on the training task in terms of the number of large errors. Children were wandering more and often 'lost track'. This is in line with an earlier study, showing selective attention impairments in children with VI (Cavezian, et al., 2012). This behaviour cannot be explained by poor acuity, because children could approach the material and optotypes were large enough to guarantee visibility (1.0 LogMAR at 40cm/ 7.0 mm). No group differences were found in number of trials performed, accuracy, performance time, and small errors. The baseline group differences in crowding ratios and large errors indicate that the material addressed those skills that are impaired in children with VI.

### **Effectiveness of Experimental Crowding Training**

Our second hypothesis was partially confirmed. We observed a striking improvement of single NVA for all training groups. The PLc training was the only training to induce an improvement of crowded NVA in both age categories (1.7 LogMAR lines). Single NVA showed an average improvement of 1.3 LogMAR lines in all training groups. When tested with the LH line 50% crowding chart, only the 4-6 year olds in the magnifier group showed an improvement (2.0 LogMAR lines). In the PL training groups LH line 50% crowding NVA improved in both categories (1.4 LogMAR lines in the PLc group and 1.2 lines in the PLu group). It is a remarkable finding that 12 training sessions can induce such a general improvement of NVA.

An explanation for the larger improvement in the PLc group is that learning effects are specific to the physical features of the stimuli in PL paradigms (Karni & Sagi, 1993; Fahle, 2004). In the PLc group children trained with optotypes with an edge-to-edge spacing that is similar to the spacing on the crowded chart we used (Haase & Hohmann, 1982; Huurneman, Boonstra, Cillessen, et al., 2012). Our paradigm did not train at threshold NVA nor did we use LH-optotypes (the optotypes we used to measure NVA), so the improvement in NVA can be seen as a transfer of the training on NVA. Generalization can occur if a *double-training paradigm* is used that combines feature learning (e.g., contrast, size) and location learning (e.g., stimulus-nonspecific factors like local noise at the stimulus location) (Zhang et al., 2010). Our PL tasks employed both mechanisms (manipulating letter size and local noise at the stimulus location).

A third component of the training tasks was the search element. The instruction of

the magnifier task was to find the inversed Landolt C. The instruction of the PL tasks was to follow the trail the inversed E's. In the two experimental training tasks, this meant disentangling small closely spaced symbols, an ability that relies on accurate eye-movements (Chung & Bedell, 1995; Vlaskamp & Hooge, 2006; Vlaskamp, et al., 2005). Our paradigm therefore was not a purely visual PL paradigm, because multiple modalities were addressed; the visual modality (visual perception, i.e., sensory processing), and motor modality (oculomotor control and fine motor skills). It is possible that the training paradigms induced task-specific improvements in the motor domain and the calibration between visual and motor skills. This would be worth studying, because motor skills of children with VI are often impaired and training could induce coupled improvements in both modalities (Reimer, Cox, Boonstra, & Smits-Engelsman, 2008; Reimer, et al., 2011).

Several possible explanations could be given for the improvements of NVA reported here. Firstly, studies show that PL does not only improve visual functions in patients with neural deficits, but also improves visual functions of patients with optical deficits (e.g., myopia : Durrie & McMinn, 2007, and presbyopia : Durrie & McMinn, 2007; Polat et al., 2012). This has led researchers to suggest that improved NVA is the result of increased efficiency of neural processing (Polat, et al., 2012). The concept of neuroplasticity, that is, the capacity to adapt and modify neural circuitry to the environment and experience (V. Anderson, Spencer-Smith, & Wood, 2011), can be seen as the underlying mechanism. Following this reasoning, the improvements found here might be associated to neuroplasticity, certainly since this capacity is considered to be substantial in childhood compared to adulthood (Bryck & Fisher, 2012).

Secondly, improved NVA might be caused by a reduction of the retinal image velocity in subjects with nystagmus, due to discovering the gaze direction entailing minimal nystagmus, also known as the null-point (Dell'Osso, van der Steen, Steinman, & Collewijn, 1992). An increase in ocular torticollis, the compensatory head turn fixating the eyes at this null-point, has been reported in children with VI after only six weeks of visual training (Reimer, et al., 2011). Although we did not monitor ocular torticollis and there was no difference in the amount of improvement between children with and without nystagmus, we cannot rule out this explanation at this point.

Thirdly, as mentioned in the introduction, PL consists of the process of increased correspondence or fidelity of perception to dimensions of stimulation (Gibson, 1963). In other words, PL pertains to an increased sensitivity for the available information from a stimulus array, more specifically, here, the relevant features of the test and training material (see e.g. Gibson, & Pick, 2000). It is not unlikely that the training made children more effective in detecting and exploiting the symbols specifying those relevant features. This improvement of attention, which may be defined as 'better knowing what to look for', is reflected by the increased NVA. This explanation is

partially backed-up by the additional decrease in large and small errors after training. On a final note, it is very well possible that these mechanisms are interrelated and influence each other. For example, a reduction in retinal image velocity enables a child to benefit from the training more, as it increases the opportunities for learning and becoming more sensitive to relevant information, as well as by increasing the efficiency of neural processing.

Crowding ratios did not decrease on a group level in any of the training conditions. However, when looking at individual data, 8 of 18 children in the PLc group, 2 of 12 in the magnifier group, and 1 of 15 in the PLu group showed a decrease of the crowding ratio. The lack of a decrease of the crowding ratio, can be explained by delayed visual maturation of single acuity in children with VI. In a previous study (Huurneman & Boonstra, in press), a stronger correlation was found between binocular single acuity and age for 4-8 year old children with albinism and infantile nystagmus syndrome ( $r = -.7$ ) than for children with NV ( $r = -.3$ ), while crowded acuities in all groups were still maturing at the same rate. These data indicate slower maturation of the visual system in children with VI. It is conceivable that more training sessions would lead to larger improvements and a subsequent reduction of the crowding ratio. This question warrants further research.

### **Generalization of Learning Effects**

Our third hypothesis was confirmed. Transfer of learning effects appeared on an untrained visual function: near visual acuity. In PL protocols that specifically focus at repeated practice at threshold sized symbols, it is to be expected that visual acuity improves (Chung, 2007). Improving contrast sensitivity in the amblyopic eye also transfers to visual acuity (Polat, 2009; Polat, et al., 2009). Transfer of functions indicates that the specificity of improvement in the training task can be generalized by repetitive practice of target detection, covering a sufficient range of spatial frequencies and orientations, leading to an improvement in unrelated visual functions. In children with amblyopia, contrast sensitivity training with Gabor patches led to an improvement of 1.5 Snellen lines on the acuity chart (Polat, et al., 2009). It is a novel finding that NVA can be improved after PL in children with VI.

### **Age Differences in Learning Effect**

Our fourth hypothesis was not confirmed. Both age groups showed an improvement in NVA on all vision charts after the PLc training. Our training task was quite a challenge for the younger children, because it demanded them to focus and sustain attention. Our tasks resemble the Eriksen flanker task (Eriksen, 1974). Adults with amblyopia also show impaired visual decision-making on Eriksen flanker tasks compared to adults with NV; these adults show significantly delayed responses (Farzin

& Norcia, 2011). In our training tasks, children had to filter out relevant (inversed E's/inversed Landolt C) from irrelevant optotypes (non-inversed E's/non-inversed Landolt C's). This basically makes it a 'conflicting' task, because distractors also undergo perceptual analysis along with the target due to imperfect selection, and they might produce additional identity-specific interference effects if they signify a response other than that designated to the target stimulus (Ridderinkhof & van der Stelt, 2000). At baseline, 6 of the 4-6 year old children with VI were unable to work with the training material. The 7-9 year olds were all able to work with the material at baseline.

An explanation for the improvement in NVA of 7-9 year-old children could be that more older children worked with smaller M-values (or print) than younger children did. This may have resulted in an equally challenging training for this group. While 14 of the 15 7-9 year olds worked with the smallest print (1M), only 9 of the 4-6 year olds did so; 5 worked with intermediate print (2M) and 4 with the largest print (4M). Thus, the task itself may have been the greatest challenge for the younger children. For the older children gain may have been related to working with the smallest optotypes which made the task challenging for them.

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**Supplement A.** *Clinical diagnosis and characteristics of children with visual impairment.*

#	Age (months)	Training	Clinical diagnosis	DVA*			NVA**	Nystagmus	Correction
				RE	LE	Bino			
1	100	PLu	Retinoschizis	2.0	0.5	0.5	0.6	no	RE S: +5.00 LE S: +5.00
2	61	PLu	Congenital nystagmus	0.8	0.8	0.9	0.8	yes	RE S: +0.25 C: -0.75 ax: 166 LE S: +0.50 C: -1.00 ax: 16
3	108	PLu	Nystagmus	0.6	0.6	0.5	0.6	yes	RE S: +3.50 C: -1.50 ax: 10 LE S: +2.50
4	74	PLc	Achromatopsia	1.0	1.0	1.0	1.0	yes	RE S: +3.50 C: -3.50 ax: 8 LE S: +3.25 C: -2.50 ax: 174
5	59	PLu	Aniridia	1.4	1.4	1.4	1.2	yes	RE S: -4.75 C: -2.00 ax: 180 LE S: -4.50 C: -1.25 ax: 5
6	86	Magnifier	Congenital Stationary Night Blindness (CSNB)	0.7	0.7	0.6	0.6	no	RE S: -3.75 C: -1.25 ax: 45 LE S: -3.50 C: -0.75 ax: 95
7	74	PLc	Oculocutaneous albinism	1.3	1.3	1.1	1.1	yes	RE S: +3.50 C: -2.75 ax: 180 LE S: +5.00 C: -2.00 ax: 176
8	74	PLc	Oculocutaneous albinism	1.0	1.0	0.9	1.1	yes	RE S: +6.00 C: -2.50 ax: 3 LE S: +3.25 C: -2.50 ax: 172
9	101	PLc	Congenital nystagmus	0.6	0.7	0.5	0.8	yes	No correction.
10	77	PLu	Congenital cataract (aphakia)	0.3	0.3	0.3	0.5	no	RE S: +3.00 LE S: +3.00
11	64	Magnifier	Oculocutaneous albinism	1.4	1.1	0.9	1.0	yes	No correction.
12	66	Magnifier	Aniridia	1.0	1.2	0.9	0.9	yes	RE S: +3.75 C: -1.50 ax: 180 LE S: +3.25 C: -2.50 ax: 174
14	104	PLu	Ocular albinism	0.9	0.9	0.9	0.9	yes	RE S: +5.50 C: -3.50 ax: 180 LE S: +5.25 C: -4.50 ax: 180

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15	106	PLc	Oculocutaneous albinism	1.0	1.0	1.0	1.0	1.0	1.0	yes	RE S: +5.25 C: -1.75 ax: 175 LE S: +5.50 C: -3.50 ax: 175 No correction.
16	84	PLu	Oculocutaneous albinism	1.0	1.0	0.9	0.8	0.8	0.8	yes	
17	104	PLu	Congenital nystagmus	0.7	0.6	0.5	0.6	0.6	0.6	yes	RE S: -2.75 LE S: -2.50
18	108	PLc	Congenital nystagmus	0.9	0.9	0.8	0.9	0.9	0.9	yes	RE S: +0.75 C: -4.75 ax:5 LE S: +0.75 C: -5.25 ax: 165
19	75	PLc	CSNB	0.7	0.8	0.7	0.6	0.6	0.6	no	RE S: -6.50 C: -1.50 ax:176 LE S: -7.00 C: -1.50 ax: 155
20	106	PLc	Congenital nystagmus	0.5	1.0	0.4	0.4	0.4	0.4	yes	RE S: +0.50 C: -2.50 ax: 14 LE S: +1.00 C: -3.75 ax: 155
22	80	PLu	Congenital nystagmus	0.4	0.6	0.4	0.4	0.4	0.4	Yes	RE S: +3.00 C: -0.75 ax: 124 LE S: +2.75 C: -1.75 ax: 32
23	61	Magnifier	Oculocutaneous albinism	1.1	1.0	0.9	0.9	0.9	0.9	yes	RE S: +6.00 C: -1.00 ax: 6 LE S: +5.00 C: -0.75 ax: 6
24	95	PLu	Congenital glaucoma	0.7	0.7	0.6	0.6	0.5	0.5	yes	RE S: -7.50 C: -1.50 ax: 118 LE S: -3.00 C: -0.75 ax: 25
25	70	PLc	Cone dystrophy	0.3	0.3	0.3	0.5	0.5	0.5	yes	RE S: -6.00 C: -1.00 ax: 2 LE S: -6.75 C: -0.75 ax: 50
26	68	Magnifier	Oculocutaneous albinism	1.1	1.1	1.0	1.2	1.2	1.2	yes	RE S: +2.00 C: -0.50 ax: 180 LE S: +3.75 C: -0.50 ax: 180
27	95	PLu	Congenital nystagmus	0.6	0.6	0.6	0.6	0.6	0.6	yes	RE S: +3.25 C: -1.25 ax: 8 LE S: +2.75 C: -1.25 ax: 180
28	61	PLc	Ocular albinism	1.1	1.1	1.0	1.1	1.1	1.1	yes	RE S: +4.00 LE S: +4.00
29	57	PLu	CSNB	0.6	0.5	0.6	0.5	0.5	0.5	no	RE S: -7.25 C: -1.25 ax: 120 LE S: -7.25 C: -1.75 ax: 75
30	92	Magnifier	Ocular motility disorder	0.6	0.6	0.5	0.5	0.5	0.5	no	No correction.
31	74	PLu	Myopia							no	RE S: -5.00 C: -3.25 ax: 2

32	61	PLu	Macular hypoplasia	0.7	0.6	0.6	0.7	no	LE S: -5.00 C: -3.25 ax: 1 RE S: +2.50 C: -2.00 ax: 177 LE S: +2.25 C: -1.75 ax: 7
33	57	PLc	Congenital nystagmus	0.6	nm	0.6	0.4	yes	No correction.
34	66	PLc	Congenital nystagmus	0.8	0.8	0.7	0.7	yes	RE S: +2.00 C: -1.00 ax: 180 LE S: +2.00 C: -1.00 ax: 170
35	109	PLc	Oculocutaneous albinism	0.5	0.6	0.4	0.4	yes	RE S: +1.50 C: -2.00 ax: 180 LE S: +1.50 C: -1.25 ax: 175
36	76	Magnifier	Congenital cataract (aphakia)	1.1	0.8	0.7	0.6	no	CL: RE:+21 G S:+2.5 C:-2.5 ax:180 CL: LE:+21 G S:+2.5 C:-1.5 ax:180
37	74	PLc	Retinal dystrophy	1.1	1.0	1.0	0.8	yes	RE S: plano C: -1.50 ax: 8 LE S: +0.25 C: -1.50 ax: 166
39	94	Magnifier	Ocular albinism	0.9	1.1	0.8	0.8	yes	RE S: +0.50 C: -1.25 ax: 105 LE S: plano C: -0.50 ax: 48
40	90	Magnifier	Congenital nystagmus	1.0	0.7	0.6	0.6	yes	RE S: +2.00 C: -1.25 ax: 172 LE S: +2.25 C: -0.50 ax: 6
41	99	PLc	Congenital nystagmus	0.4	0.4	0.4	0.3	no	RE S: +4.50 LE S: +3.50 C: -0.50 ax: 180.
42	85	PLc	Achromatopsia	1.3	1.3	1.1	1.2	yes	RE S: +4.00 C:-0.75 ax:180 LE S:+3.00
43	106	PLu	Ocular albinism	1.0	0.8	0.5	0.5	no	RE S: +6.00 C: -1.00 ax: 150 LE S: +4.25 C: -0.50 ax: 180.
44	79	Magnifier	Congenital nystagmus	0.8	1.0	0.5	0.5	yes	RE S: +2.00 C: -1.50 ax: 130 LE S: +3.00 C: -1.50 ax: 160
45	75	Magnifier	Ocular albinism	1.4	1.0	1.0	1.1	yes	RE S: +4.25 C: -2.50 ax: 10 LE S: +4.75 C: -2.00 ax: 170
46	66	PLc	Ocular albinism	0.8	0.8	0.8	0.7	no	RE S: +3.50 C: -1.25 ax: 177 LE S: +3.00 C: -1.25 ax: 172
47	95	Magnifier	Ocular albinism					yes	RE S: +1.75 C: -2.00 ax: 5

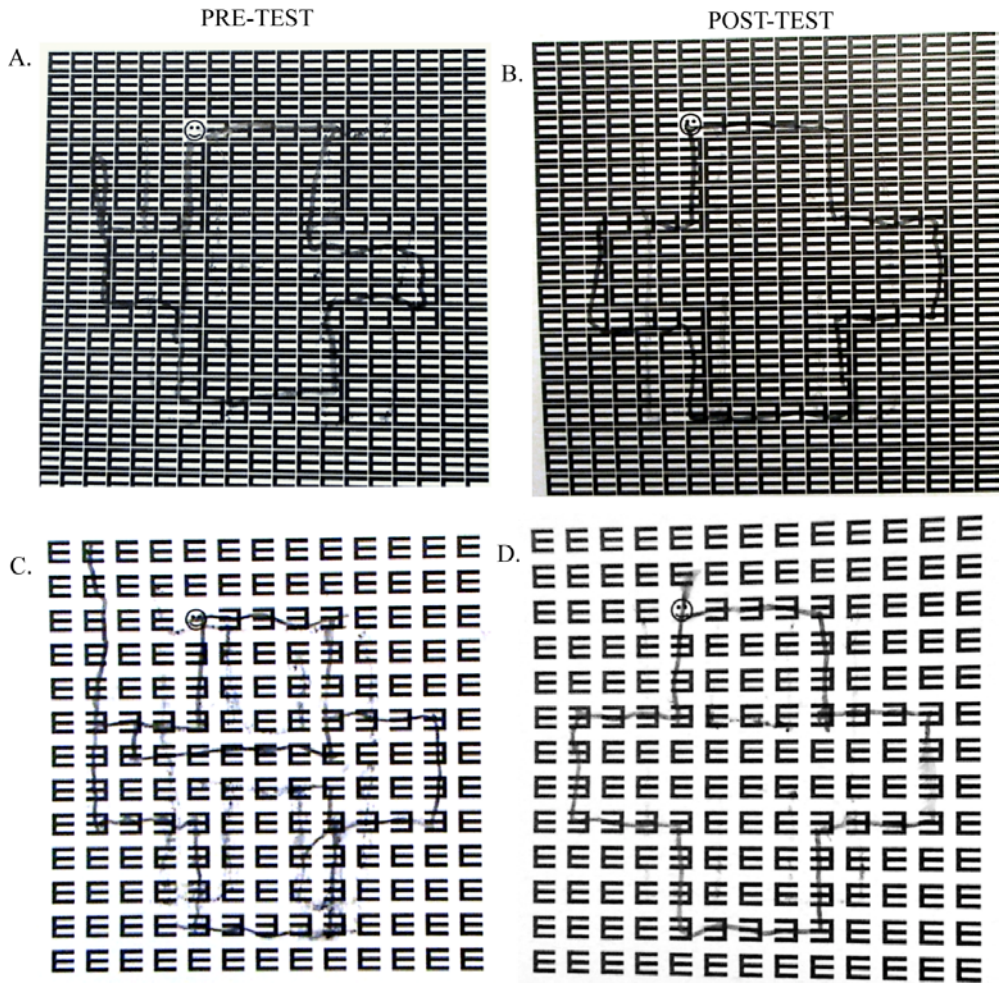


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48	62	PLc			1.1	1.1	0.8	0.9		LE S: +2.75 C: -2.50 ax: 172 RE S: +1.00 LE S: +1.50
			Congenital nystagmus		0.8	0.7	0.7	0.8	yes	

\* Distance visual acuity (DVA) with C-test crowded version 2.6' spacing at 5 m (LogMAR).

\*\* Near visual acuity (NVA) measured with C-test crowded version 2.6' spacing at 40cm (LogMAR).



**Supplement B** A) Presents a figure drawn by a six-year old boy during pre-test and (B) presents an example of post-test performance. (C) Presents an example of a figure drawn during pretest for a six-year-old boy in the PLu group at pre-test and (D) presents an example of post-test performance.

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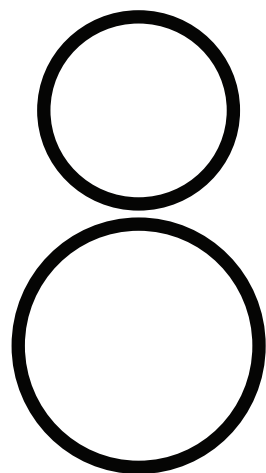
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chapter

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General  
discussion







## GENERAL DISCUSSION

This chapter summarizes the main findings that can be drawn from this thesis. The first section will cover the four main themes of this thesis (presented in Chapter 1). The second section presents three clinical implications arising from the results of the studies presented in this dissertation. The last section provides directions for future research.

### 1. Crowding ratios

#### 1.1 Chart design and group differences

Crowding ratios can be calculated by dividing the single optotype acuity with the linear optotype acuity (Rydberg, et al., 1999). When crowding ratios are  $>1.00$ , this indicates that the presence of distracting letters degrades visual acuity. Binocular crowding ratios for near and distance vision were measured with clinically available vision charts: a chart with fixed spacing and a chart with proportional optotype spacing (Chapter 2). The influence of group, age, and nystagmus was measured. Three important results were found: (i) crowding ratios were higher in children with visual impairment (VI) than in children with normal vision (NV), (ii) there was no age-related decline of crowding ratios in children with VI (which was observed in children with NV), and (iii) crowding ratios were higher in children with VI accompanied by nystagmus (VI+nys) than children with VI without nystagmus (VI-nys). Only charts with fixed spacing differentiated between groups, ages, and nystagmus.

Test design might explain the higher crowding ratios measured with the fixed charts. The charts with fixed spacing possibly evoked *more crowding at the lower acuity range*, because spacing is relatively smaller in this range (Haase, 1993). However, children with NV also showed higher crowding ratios when measured with charts with fixed spacing in comparison with proportional charts (if decimal crowded near visual acuity  $\geq 0.50$ : spacing proportional chart 25% crowding is  $\leq 2.5$  arc min ( $^{\circ}$ ); and  $2.6'$  for the fixed chart). Therefore, spacing does not seem to be the only explanation. Another explanation for the different outcome between the two tests is the *number of distracting optotypes*. The proportional charts present 2-5 optotypes standing next to each other, whereas the fixed test presents 12 optotypes on each line for acuities 20/200 and better (which was the case in 45/58 of the children with VI). More characters standing next to each other could lead to stronger interference.

#### 1.2 The influence of (additional) nystagmus on crowding ratios

The second factor associated with higher crowding ratios was nystagmus. Children with VI+nys showed higher crowding ratios than children with VI-nys. Crowding ratios of children with VI-nys and children with VI+nys were compared while

controlling for acuity. The crowding ratios of the VI+nys group remained higher than those found in the VI-nys group, even after controlling for acuity. Our explanation for this finding is that fixational instability contributed to the higher crowding ratios. While this is the first study to report higher crowding ratios in children with VI+nys, it was already known that adults with congenital nystagmus experienced excessive contour interaction effects (Chung & Bedell, 1995; Pascal & Abadi, 1995). Two previous studies provided explanations to account for extensive contour interaction in adults with congenital nystagmus: greater retinal image motion, and the higher prevalence of sensory amblyopia. The impact of amblyopia on object recognition should not be underestimated, as it has also been described as a developmental disorder of cortical origin (Hussain, Webb, et al., 2012) associated with higher-level visual processing deficits (Sharma, Levi, & Klein, 2000).

### **1.3 Mono- and binocular crowding ratios**

Mono- and binocular crowding ratios for distance vision were compared in three groups of children: children with albinism (with and without nystagmus), children with (idiopathic) infantile nystagmus syndrome (INS), and children with NV (Chapter 6). Mono- and binocular crowding ratios were higher for children with INS than for children with NV. In other words, the INS group showed higher crowding ratios under *all* viewing conditions. For children with albinism, the binocular crowding ratio and the crowding ratio in the poorer eye were higher than those of children with NV. Children with albinism and children with INS showed larger interocular acuity differences than children with NV (0.1 log unit in our clinical groups and 0.0 log unit in children with NV). Strabismus and nystagmus amplitude significantly predicted the crowding ratio in the poorer eye in our two clinical groups.

In sum, crowding ratios are higher in children with VI than in children with NV when measured with charts with fixed spacing. Specific clinical features, i.e. nystagmus characteristics and the presence of strabismus, seem to be associated with stronger crowding effects.

## **2. Stimulus characteristics**

### **2.1 Spacing**

As described above, crowding effects are obviously stronger when spacing is smaller and when there are more distractors surrounding the target (Chapter 2). Another stimulus characteristic that might explain crowding is the configuration of the stimulus (see section 2.2), but it should be mentioned that spacing effects are dependent on stimulus configurations. For example, when children with NV search in a row with homogeneous distractors, smaller spacing will facilitate search times (section 2.2.1).

However, in a matrix configuration, smaller spacing does not facilitate search times and degrades search performance (section 2.2.2).

## **2.2 Configuration**

### **2.2.1 Row**

Configuration influenced the effect of element spacing (Chapter 5). During row search with homogeneous distractors (simple search), small spacing did not cause a drop in performance measures. Smaller spacing even facilitated simple row search performance of children with NV: their reaction times were up to 40% shorter for trials with smaller spacing. This latter finding is consistent with studies in adults with NV indicating that patterns with discriminable elements in close proximity can be segregated more easily than patterns with more widely spaced elements (Nothdurft, 1985, 1993; Scolari, et al., 2007). In children with VI, this facilitating effect of smaller spacing was absent.

### **2.2.2 Matrix**

In contrast, during simple matrix search (homogeneous distractors) smaller spacing had a negative impact on performance. The VI+nys group was less accurate at 2' and 4' element spacing than children with NV. Secondly, this adverse effect of small spacing on accuracy was not only observed by between-group differences, but also by within-group differences: all groups were slower at smaller spacings during simple search. In addition, children with VI (both groups) were up to 5-fold slower than children with NV during simple matrix search.

## **2.3 Distractor-distractor similarity**

During complex matrix search (that is, visual search with heterogeneous distractors), the accuracy of the VI+nys group was impaired until spacing was at least larger than 16'. This indicates that group differences are more extensive for complex (heterogeneous distractors) than simple (homogeneous distractors) matrix search. Search performance is disproportionately poorer for children with VI compared to children with NV on a serial search task. Our explanation for this effect of distractor-distractor similarity is not that selective attention is especially poor, because group difference disappeared at the largest spacing. We suspect that oculomotor control plays a key role during search, because serial search is more dependent on accurate eye movements than parallel search (Young & Hulleman, 2013). We suspect that the poorer performance of children with VI+nys is a result of an inability to adjust saccade size and to fixate steadily. Children with NV showed consistent adaptation of eye movements on stimulus characteristics, but we did not observe these adaptive abilities as strongly in our VI groups and think oculomotor control can be seen as a prerequisite to perform serial search tasks with small, closely spaced symbols.

#### 2.4. Spacing and oculomotor strategies

Oculomotor measures in the NV and VI+nys group differed in two ways: (i) children with VI+nys made more fixations than children with NV, and (ii) children with VI+nys made larger saccade amplitudes than children with NV at the smallest spacing. The oculomotor strategy found in children with VI+nys deviates from the strategy observed in children with NV and previous studies in adults with NV reporting smaller saccade amplitudes at smaller spacings (Vlaskamp & Hooge, 2006; Vlaskamp, et al., 2005). The oculomotor strategy observed in the VI+nys group might be best explained by their greater need for refixations due to the presence of retinal slip. More refixations (Kanonidou, et al., 2010) and larger saccade amplitudes (Shi, et al., 2012) have also been reported in adults with amblyopia. In children with VI-nys, no differences were observed in oculomotor recordings compared to children with VI+nys and children with NV, but this might be (at least partially) attributable to the small sample size of children with valid oculomotor recordings (n=4-6).

The following stimulus characteristics are associated crowding: (i) number of distractors, (ii) configuration, and (iii) heterogeneous distractors. The presence of nystagmus, again, was associated with stronger crowding.

### 3. Magnification and crowding

We compared the influence of two different types magnification (magnifier vs. large print) on crowded task performance (Chapter 4). In daily classroom situations, teachers often give students with VI large print instead of providing them with magnification. However, two practical advantages of a magnifier over large print are that magnifiers enable children to inspect any written information at normal print size, and are less expensive than producing large print books. In this study we divided children into two age groups (4-6 year olds and 7-8 year olds) and two experimental conditions (magnifier versus large print) in order to investigate how age and type of magnification affect crowded task performance.

The conclusion of this study was that a magnifier and large print are equally effective in improving the performance of young children with a range of visual acuities on a crowded near vision task. Curiously, children with stronger crowding effects showed larger improvements when working with magnification. This might be explained by the *increase of absolute spacing* on the crowded near visual acuity chart. The small, fixed spacing of 2.6' on the unmagnified version of the chart might have been the bottleneck when the child named the optotypes without magnification. When providing magnification on a chart with fixed spacing, the size of the optotype and spacing between optotypes increases and the spacing-bottleneck was thereby removed. Eight children (average crowding ratio 1.9) showed larger improvement of crowded

near visual acuity than was expected based on their totally received magnification (distance magnification (by reducing viewing distance) + magnification provided by large print or magnifier).

The greater improvements observed in children with higher crowding ratios can be attributed to the magnification of absolute spacing. For example, a magnification factor of  $1.8\times$  enlarges (fixed chart) spacing from 2.6' to 4.7'. Distance magnification can be added to this, and together this removes spacing as a bottleneck. Theoretically, it is not to be expected that a magnifier would decrease crowding on charts with proportional spacing, because on these charts spacing scales with optotype size.

#### **4. Intervention: Reduction of crowding by perceptual learning**

Perceptual learning (PL) can reduce crowding effects in the amblyopic fovea and in the normal periphery (Chapter 3). PL is based on the notion that practicing visual tasks can lead to dramatic and long-lasting improvements in performing these tasks (Huckauf & Nazir, 2007). The reviewed studies showed that PL can reduce critical spacing (or contour interaction areas), improve visual acuity, contrast sensitivity, ocular alignment and efficiency of non retinotopic higher brain processes engaged in attention and decision making.

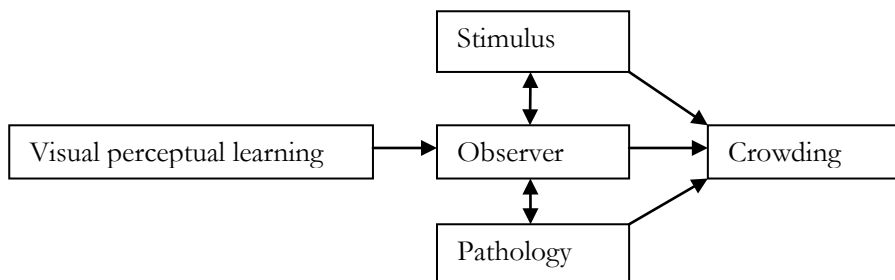
Based on the knowledge collected from previous work, both that of others and our own, an intervention was developed (Chapter 7). Certain stimulus characteristics played a crucial role in evoking stronger crowding effects: spacing, stimulus configuration (matrix), number of distractors, and distractor-distractor identity (heterogeneous distractors). Nystagmus and visual attention were important observer characteristics. Our training paradigm was designed based on these factors and consisted of training material with small spacing, a matrix configuration, a visual search component, and a demand on element-by-element scrutiny (and therefore poses a demand on the ability to make fine eye movements). The effectiveness of three training paradigms was compared. The PL training required children to (i) search in a grid sized  $145\times 145$  mm consisting of illiterate E's for the smiley, (ii) follow the trail of inversed optotypes (originating from the smiley), and (iii) draw an exact line across the inversed optotypes trail (guaranteeing that children looked carefully at the stimulus and selectively filtered the target symbols from distractors). There was an experimental PL group that worked with edge-to-edge element spacing of 0.3 mm ( $0.04^\circ$  at 40 cm; consistent with spacing of the crowded chart of the C-test), and a control PL group working with an uncrowded version, with spacing of 3.6 mm ( $0.52^\circ$  at 40 cm; consistent with spacing of the single chart of the C-test). The magnifier group trained with a 191 mm array containing three rows with Landolt C's sized 0.5 mm ( $0.32$  M or  $-0.1$  LogMAR at 40 cm) with an edge-to-edge element spacing of 0.3

mm. Children had to search for the inversed Landolt C in this row with an electronic handheld magnifier with a display size of 3.5", providing  $8\times$  magnification.

The aim of this intervention was to reduce crowding and improve near visual acuity in children with VI. Four important observations were made during this study: (i) there were baseline differences: children with VI had higher crowding ratios and made more large errors on the training task than children with NV (the large errors indicate that the children with VI more often 'lost track' than children with NV), (ii) we found striking improvements of single NVA in all training groups (1.3 LogMAR line on average), (iii) the experimental PL group was the only training that induced an improvement of crowded NVA in both age categories (4-6 years and 7-9 years; 1.7 LogMAR line on average), and (iv) we found no decrease of crowding ratios in any of the training groups. There are indications that children with VI experience delayed maturation of single visual acuity compared to children with NV (Chapter 6). This delayed maturation may account for the lack of a reduction of the crowding ratio.

### **In sum: training as a compensation for degraded visual input**

Below, Figure 8.1 presents a schematic representation which captures our main findings: ocular disease has an adverse impact on early stages of perception (such as visual acuity; which depends primarily on the quality of retinal information ascending from the retina to the visual cortex), but also the degree of foveal crowding, search speed, and accuracy of search in crowded displays (functions that rely on extrastriate areas and attentional feedback mechanisms).



**Figure 8.1** *Perceptual learning causes direct specific learning effects on a trained task. An indirect effect may be that newly acquired skills (such as improved visual attention or improved fixational eye movements) may indirectly improve visual functions that are damaged due to pathology (such as near visual acuity and fixational stability).*

Our research indicates that within the population of children with VI there are clinical features that are associated with relatively higher amounts of crowding: the presence of strabismus and the presence of nystagmus. The majority of children with VI

experience nystagmus and there is also a higher prevalence of strabismus. These conditions cause suppression (in case of amblyopia) or retinal slip (in case of nystagmus) of incoming visual input, leading to poorer spatial resolution.

PL caused improvements in near visual acuity scores, but none of the child characteristics (pathology, age, amount of trials practiced, baseline acuity, or size of stimuli) could account for the amount of improvement in near visual acuity that was observed. We suspect that the characteristics of the eye are probably not improved by PL, but perceptual and attentional networks are both influenced by repetitive exposure to small stimuli requiring attentive filtering. We suspect that PL directly causes improvements on the trained task by specific learning effects, but there might be an indirect learning effect on skills such as visual attention and fixational stability that are responsible for a transfer of learning effects on functions that are impaired due to pathology.

## **Implications for clinical practice**

Three main clinical implications arise from this thesis. The first is that charts with fixed spacing show higher crowding ratios in children with VI compared to children with NV and are more sensitive in detecting crowding. The second is that certain clinical features (e.g. nystagmus frequency and amplitude) are associated with stronger crowding. The third is that children with VI benefit from PL; which is expressed in a higher NVA in VI after PL training.

### **1. Fixed or proportional charts?**

#### **1.1 Fixed charts**

The charts with fixed spacing were designed by Haase and Hohmann, in the 1982 (Haase & Hohmann, 1982; Hohmann & Haase, 1982). They suggested that spacing should be fixed, because “proportional measures do not take into account the well known exaggerated interaction between neighbouring contours in amblyopia” and “the quality of screening for testing visual acuity disorders is unsatisfactory” (Hohmann & Haase, 1993). Haase reasoned that, the small interspacing between letters of the acuity steps in the higher resolution area may induce crowding, whereas the larger spacing between greater optotypes can avoid contour interaction. The C-test, with its fixed optotype spacing, is an often used clinical chart (Graf, et al., 2000; Haase & Hohmann, 1982; Neu & Sireteanu, 1997). One of the advantages of the C-test is its strong sensitivity to pick up amblyopia and uncorrected refractive errors demonstrated by the lower percentage of false negatives reported with the C-test (5%) than reported with regular acuity charts (48% : Hohmann & Haase, 1993).

#### **1.2 Proportional charts**

Others proposed that visual acuity charts should use proportional spacing. The first studies which quantified foveal contour interaction effects were conducted by Flom (Flom, Heath, et al., 1963; Flom, Weymouth, et al., 1963). These studies demonstrate that adjacent contours can induce considerable interference when they are placed within an area of 2 times the gap width of the testing letter. Flom stated that crowding is related to the size of the receptive fields, i.e. the restricted portion of the visual field to which neurons respond, that are most sensitive to the target. The *scale-shift hypothesis* (Flom, Heath, et al., 1963; Flom, Weymouth, et al., 1963) predicts that the interaction zone depends on visual acuity and lower visual acuity is associated with the engagement of larger receptive fields, and this “scale-shift” will result in proportionally larger crowding distances.



### 1.3 Foveal crowding in amblyopia and during development

In the amblyopic fovea, crowding effects do not appear to be scale-invariant: the extent of interaction (expressed in MAR) is larger for small targets (Hess, Dakin, Tewfik, & Brown, 2001; Levi, Hariharan, & Klein, 2002; Levi & Klein, 1982a, 1982b). In the normal fovea, enlarging the threshold sized optotype with  $\frac{1}{2}$  LogMAR line already removes contour interaction (Chung & Bedell, 1995). In adults with congenital nystagmus enlargement of 1.1 LogMAR line is sufficient to remove contour interaction effects when flanking bars are placed at 2 MAR from the target (Chung & Bedell, 1995). There are no direct studies which have independently measured both the crowding extent and magnitude in children, but it is known that contour interaction areas are 1.5-3 $\times$  larger than in adult NV and crowding magnitudes are also larger, that is 1-2 lines on an acuity chart (Huurneman, Boonstra, Cox, et al., 2012).

In sum, studies have reported satisfactory sensitivity for charts with fixed spacing (Hohmann & Haase, 1993). For now, our advice is to use the fixedly spaced charts in a clinical setting, because when measured with proportionally spaced charts, the influence of developmental effects (age) and nystagmus on crowding ratios, as described in psychophysiological experiments in patients and children, are not measured. Furthermore, others have said that “The main purpose of visual acuity assessment in children is to detect amblyopia and to control its treatment” (Graf, et al., 2000). There are indications that this goal might be best attained by using sensitive charts (Graf, et al., 2000; Haase & Hohmann, 1982; Hohmann & Haase, 1993).

## 2. Clinical characteristics associated with crowding

Fixation instability due to nystagmus contributes to enhanced crowding. It was difficult to compare children with and without nystagmus, because many children with VI experience nystagmus. In the group of children with VI we saw in 2010, 38 out of 58 children had nystagmus (66%). In the group of 2012, the vast majority of the children (33/45) had nystagmus (73%). Our first study on crowding ratios indicated differences between these groups: the VI-nys groups showed lower crowding ratios than the VI+nys group, even when controlling for their single visual acuity.

### 2.1 Nystagmus amplitude

Nystagmus amplitude was the strongest predictor of the crowding ratio in the poorer eye in our clinical group. As earlier work also demonstrated (Abadi & Bjerre, 2002), we found no differences in nystagmus amplitudes between the group with albinism and the idiopathic INS group (mean amplitudes respectively 6.2° and 5.8°). The linear regression analysis showed that higher nystagmus amplitudes were associated with higher crowding ratios in the poorer eye.

## 2.2 Strabismus

The presence of strabismus also predicted the crowding ratio in the poorer eye. This may not be a shocking finding, since there is ample of evidence that strabismus is associated with extensive crowding (Greenwood, et al., 2012; Levi, et al., 2002; McIntyre, 1992). However, our study is the first to address the relation between strabismus in VI and crowding. Strabismus can exert a major influence on visual development ranging from a complete absence of stereopsis (Sireteanu, 2000) to poor eye hand-coordination (Niechwiej-Szwedo, Goltz, Chandrakumar, & Wong, 2012) and higher-level visual processing deficits (Sharma, et al., 2000). Evidence is accumulating that an operation is often not suffice (Pineles, Ela-Dalman, Zvansky, Yu, & Rosenbaum, 2010) to improve sensory functions. It is the job of clinicians to transfer this knowledge to their patients and offer them rehabilitation programs focused at improving sensory functions.

## 2.3 Nystagmus frequency

There was a consistently strong relation between crowding ratios and nystagmus frequency in children with idiopathic INS in all viewing conditions. Nystagmus frequency was significantly higher in the children with INS than in children with albinism (mean frequencies respectively 4.9 Hz and 3.7 Hz), replicating earlier work (Kumar, et al., 2011). Nystagmus frequency is related to foveation duration and there is a direct relation between foveation duration and visual acuity (Simmers, et al., 1999). However, simulation of retinal image motion in adults with NV shows that this shorter foveation duration does not fully account for the observed contour interaction in INS (Chung & Bedell, 1995).

## 2.4 Anisometropia

Finally, anisometropia defined as the difference in dioptres of spherical refraction between the two eyes showed a positive correlation with the crowding ratio in the better eye. However, this correlation was fairly weak compared to the other patient characteristics ( $r=0.26$ ). This lack of a relation may be explained by a restricted range (only 5 subjects in our clinical group had spherical interocular differences  $> 1D$ ).

## 3. Improving near visual acuity by a period of PL

PL seemed to be an effective visual training method to stimulate the development of near visual acuity in children with VI. Only 12 sessions of PL during 6 weeks already induced a remarkable improvement of near visual acuity. We also observed a reduction of the crowding ratio in 8 out of 18 children with VI, but this reduction did not reach significance. Children with VI had higher crowding ratios and showed a higher amount of large errors compared to children with NV. The amount of large

errors was associated with degree to which children lost track. These errors were reduced after training with factor 4, which indicates improved focused attention and specific learning effects. Visual functions in children with VI can be improved by a highly structured, challenging protocol. Because children with VI, especially those with albinism and idiopathic nystagmus, are at risk of delayed maturation of acuity this intervention should be adopted by rehabilitation specialists.

In sum, clinicians should be aware of the clinical characteristics that predict stronger crowding and promote the use of visual training paradigms. This is important, because recent studies have shown that children with VI (idiopathic nystagmus and albinism) have a need for optotype sizes that are far beyond their acuity threshold to achieve optimal reading speed (Barot, et al., 2013; Merrill, et al., 2011). With a “head-start” provided by an intense visual attention training that improves visual acuity, they might be able to achieve faster reading speeds with smaller fonts. This question warrants further research.

**Directions for future research**

As can be gathered from the section above, this work has answered several questions about the clinical measurement of crowding, visual search and crowding, the role of eye movements in crowding, the influence of magnification on crowding, and the influence of PL on the improvement of near visual acuity and reduction of crowding effects in children with VI. Below, directions for future research are presented.

**1. The value of prolonged training**

The first issue that needs further research is the possible additional value of a prolonged training period (e.g. Hussain, Webb, et al., 2012). A period of training on a challenging task induces improvements in near visual acuity (Chapter 7). However, it did not reduce crowding ratios significantly on a group level. This reduction would be desirable, because the crowding ratio represents the capacity of a visual system with any given resolution capacity to resolve cluttered image as good as single images (like the normal adult visual system). While there were 8/18 children which showed a reduction, there were 10 children not showing a reduction or even showing an increase. Of the 8 children that did show a reduced crowding ratio after training, the majority of this group (5 out of 8) consisted of 8-9 year old boys with albinism or idiopathic nystagmus. Their average crowding ratio decreased from 1.86 at pretest to 1.32 at posttest. It could be speculated that the single acuity of these children was mature and the crowded PL training further improved crowded near visual acuity. In the other groups only 1 or 2 children showed a reduction of their crowding ratio. It is unknown whether prolonged training could induce further improvements in near visual acuity and a significant reduction of the crowding ratio on a group level.

**2. The relation between reading and crowding in children with VI**

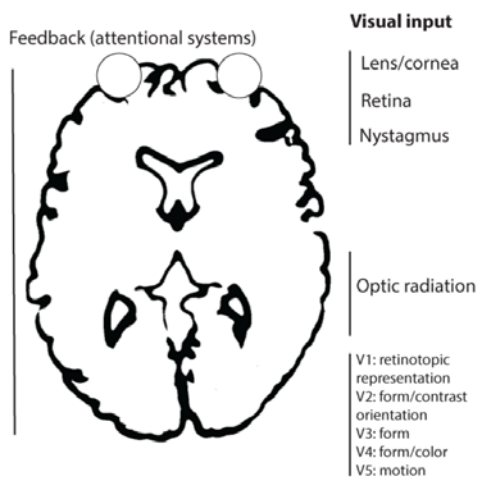
Second, our work warrants future research investigating the relation between reading and crowding. Although we did not measure reading performance in this population of children, we did find strikingly longer search times in children with VI compared to children with NV. Previous research in adults with VI showed that search speed predicts reading speed (MacKeben & Fletcher, 2011). Slower reading speed has been reported in children and adults with albinism (Merrill, et al., 2011), adults with INS (Thomas, et al., 2011), and adults with strabismus (Kanonidou, et al., 2010). In order to reach maximum reading speed they need much larger print than expected based on their NVA (on average 0.31 log units in albinism : Merrill, et al., 2011, up to 0.6 log units in INS, and 0.16 units in NV : Barot, et al., 2013; Subramanian & Pardhan, 2006). The lower reading speed might be (partially) attributed to the larger font size (Legge, et al., 2007), and more saccades due to enlargement (Dickinson & Fotinakis, 2000). The relation between near visual acuity and reading speed makes it interesting

to investigate whether reading speed (and search speed) can be improved after a period of PL.

### 3. Neural origin of crowding and learning in children with VI

Third, brain imaging studies may provide useful insights into the relation between crowding and ocular pathology. The locus of crowding on a neural level is unclear, but includes suppression of V1 activity (Millin, Arman, Chung, & Tjan, 2013), and (increased) suppression of extrastriate visual areas (V1-V4: Anderson, Dakin, Schwarzkopf, Rees, & Greenwood, 2012 ; V2-V3: Bi, Cai, Zhou, & Fang, 2009, see Figure 8.2). The visual cortex reorganizes in response to abnormal visual input. In patients with achromatopsia, the several square centimetres of the striate cortex associated with responding to foveal input in controls with NV, responds to rod input, while this region was inactive in controls under rod viewing conditions (Baseler et al., 2002; Morland, Baseler, Hoffmann, Sharpe, & Wandell, 2001). Albinism is associated with misrouting of optic fibres at the optic chiasm, which results in cortical remapping of V1 and V2 (Wolynski, Kanowski, Meltendorf, Behrens-Baumann, & Hoffmann, 2010). During ‘steady fixation’ patients with albinism showed superior colliculus activity (perhaps to compensate for retinal image slip) and larger activated cortical areas (due to expanded retinal areas), which might be attributed to the presence of nystagmus (Schmitz et al., 2004). In addition, reduced activity was observed in the most posterior aspects of V1 in subjects with albinism. This part of the visual cortex represents the most central part of the retina and could be caused by foveal hypoplasia in subjects with albinism, leading to reduced activation of these areas. The last example of cortical reorganization is amblyopia, which results in reduced activity in V1 and V2, and increased deficits from lower to higher level visual areas (Li et al., 2013; Thompson, Villeneuve, Casanova, & Hess, 2012).

These studies demonstrate that ocular disease not only entails the eye, but also alters



the cortical architecture. Knowledge about visual processing at a neural level might give further insights into the relation between VI and crowding. Future research should evaluate how crowding can be explained on a neural level and how training alters neural activity.

**Figure 8.2** *Visual crowding has been associated with reduced activity in areas V1-V4.*

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The image features a decorative border of dark blue triangles arranged in a grid pattern. The triangles are oriented with their bases at the bottom and their apexes pointing upwards. The word "Appendix" is centered within this border, rendered in a black, serif font. The background behind the text is a light gray color, which contrasts with the dark blue of the triangles and the white background of the page.

Appendix



## NEDERLANDSE SAMENVATTING

Crowding is een fenomeen dat optreedt wanneer objectherkenning wordt belemmerd door de aanwezigheid van omliggende objecten en beperkt daarmee onze visuele waarneming. Het fenomeen is in sterke mate aanwezig in onze perifere retina en komt slechts in geringe mate voor in de fovea van goedziende volwassenen. Het was al bekend dat bij kinderen crowdingeffecten sterker zijn dan bij volwassenen. Crowding kan daarom worden gezien als een ‘normaal’ ontwikkelingsfenomeen en als één van de redenen waarom letters in tekstboeken voor jonge kinderen groter moeten zijn en waarom jonge kinderen trager lezen (Jeon, Hamid, Maurer, & Lewis, 2010). Deze dissertatie richt zich op het meten en manipuleren van crowding bij 4-9 jarige goedziende (GZ) en slechtziende (SZ) kinderen. De mogelijkheid om stabiel en nauwkeurig te fixeren, ontwikkelt zich tot in de adolescentie (Äring, Grönlund, Hellström, & Ygge, 2007). Ook is de selectieve visuele aandacht nog ‘onrijp’ bij jonge kinderen (Woods et al., 2013). De centrale vraag in dit proefschrift is: In hoeverre beïnvloedt slechtziendheid de mate van crowding bij kinderen?

Stabiele fixatie en selectieve visuele aandacht zijn van groot belang voor het reduceren van crowding en hebben nadrukkelijk extra aandacht gekregen in dit proefschrift (voor oogbewegingen: zie Hoofdstuk 2, 5, en 6; voor selectieve visuele aandacht: zie Hoofdstuk 5 en 7). Daarnaast is er gezocht naar interventies die crowding kunnen verminderen. We hebben een systematische review hierover geschreven, de invloed van vergroting gemeten, en uiteindelijk een interventie ontwikkeld en geëvalueerd (zie Hoofdstuk 3, 4, en 7). Deze samenvatting zal de belangrijkste bevindingen binnen vier onderzoeksthema's presenteren. De onderzoeksthema's zijn: (i) Crowding ratio's, (ii) Stimuluseigenschappen, (iii) Vergroting en crowding, en (iv) Interventie op basis van perceptual learning.

### 1. Crowding ratio's

**Hoofdstuk 2** rapporteert over crowding bij 4-8 jarige GZ ( $n = 75$ ) en SZ ( $n = 58$ ) kinderen. De uitkomstmaat die wordt vergeleken, is de crowding ratio. Crowding ratio's kunnen berekend worden door de single visus, de visus voor losse symbolen, te delen door de crowded visus, ofwel de visus voor symbolen in de rij (Rydborg et al., 1999). Wanneer een crowding ratio groter is dan 1.00 betekent dit dat door de aanwezigheid van omliggende optotypen de crowded visus lager is dan de single visus. Vijf klinisch visuskaarten werden gebruikt: de C-test (Hohmann & Haase, 1982), de LH versie van de C test, de LH 100% crowding test, de LH 50% crowding test en de LH 25% crowding test (Hyvärinen, Näsänen & Laurinen, 1980). De eerste tweegenomde zijn testen met absolute spacing, d.w.z. de afstand tussen de optotypen

is niet gerelateerd aan de optotype grootte, en de laatste drie zijn proportionele testen waarbij de afstand proportioneel is aan de grootte van het optotype.

### 1.1 Visuskaartontwerp en groepsverschillen

De visuskaarten met absolute spacing lieten significant hogere crowding ratio's zien voor SZ dan GZ kinderen (zowel op 40 cm als 5 m). De leeftijdsgerelateerde afname van crowding voor de nabijvisus die gezien werd bij GZ kinderen wanneer zij getest werden met visuskaarten met absolute spacing was niet aanwezig bij de SZ kinderen. De kaarten met een relatieve spacing lieten geen verschil zien tussen GZ en SZ kinderen; evenmin werden met deze kaarten leeftijdseffecten gemeten. Het ontwerp van de visuskaart kan een verklaring zijn voor de hogere crowding ratio's die gemeten zijn met de visuskaarten met absolute spacing. Bij de kaarten met absolute spacing ontstaat meer crowdingeffect bij de kleine optotypen (Haase, 1993). GZ kinderen laten echter ook hogere crowding ratio's zien wanneer ze gemeten worden met een kaart met absolute spacing dan wanneer ze gemeten worden met een kaart met proportionele spacing. We stellen vast dat bij het meten van crowding de kaarten met absolute spacing een gevoeliger meetinstrument zijn. Een voorbeeld: wanneer de decimale crowded nabijvisus  $\geq 0.50$  is ( $\leq 0.30$  LogMAR), dan hebben proportionele kaarten met 25% crowding  $\leq 2.5'$  (boogminuten) spacing; en is spacing  $2.6'$  bij de kaart met absolute spacing. Spacing is niet de enige verklaring voor het verschil in uitkomst tussen de visuskaarten met absolute en proportionele spacing. Een tweede verklaring voor het verschil in uitkomst tussen de testen, is het aantal omliggende optotypen. De proportionele kaart presenteert 2-5 optotypen die direct naast elkaar staan, terwijl de kaart met absolute spacing 12 optotypen naast elkaar presenteert voor een visus van 20/200 of beter (wat het geval was in 45 van de 58 SZ kinderen). Meer optotypen direct naast elkaar zou kunnen leiden tot sterkere interferentie-effecten.

### 1.2 Nystagmus

SZ kinderen met nystagmus hadden hogere crowding ratio's dan SZ kinderen zonder nystagmus, zelfs na het controleren van verschillen in visus. Een verklaring voor deze bevinding is dat fixatie-instabiliteit een bijdrage levert aan hogere crowding ratio's. Onze studie is de eerste die hogere crowding ratio's laat zien bij SZ kinderen met nystagmus. Er was al eerder gerapporteerd dat volwassenen met congenitale nystagmus excessieve contourinteractie ervaren (Chung & Bedell, 1995; Pascal & Abadi, 1995). De verklaringen hiervoor zijn retinale beeldbeweging, en een hogere prevalentie van sensorische amblyopie. De impact van amblyopie op objectherkenning zou niet onderschat moeten worden, omdat amblyopie ook wel wordt beschreven als visuele ontwikkelingsstoornis met een corticale oorsprong (Hussain, Webb, Astle, &

McGraw, 2012), geassocieerd met problemen met hogere niveaus van visuele informatieverwerking (Sharma, Levi, & Klein, 2000).

### 1.3 Mono- en binoculaire crowding ratio's

In **Hoofdstuk 6** werden interoculaire verschillen in gezichtsscherpte en mono- en binoculaire crowding ratio's voor de vertevisus vergeleken in drie groepen kinderen: kinderen met albinisme (met en zonder nystagmus [n=16]), kinderen met (idiopathische) nystagmus (IN [n=10]), en GZ kinderen (n=72). Metingen werden gedaan met de C-test, een test met absolute spacing (Hohmann & Haase, 1982). Met behulp van een lineaire regressieanalyse werd de bijdrage van vijf voorspellers op de mono- en binoculaire crowding ratio's geëvalueerd: nystagmus amplitude, nystagmus frequentie, strabismus, astigmatisme, en anisometropia. Mono- en binoculaire crowding ratio's waren hoger bij kinderen met IN dan bij GZ kinderen. Met andere woorden, de kinderen met IN lieten hogere crowding ratio's zien onder *alle* kijkomstandigheden. Kinderen met albinisme lieten hogere crowding ratio's zien in het oog met de laagste visus en hadden hogere binoculaire crowding ratio's dan GZ kinderen. Kinderen met albinisme en IN lieten grotere interoculaire verschillen zien dan GZ kinderen (de mediaan bij de klinische groepen was 1 LogMAR regel verschil en bij 0 LogMAR regels bij GZ kinderen). Strabismus en nystagmus amplitude waren significante voorspellers van de crowding ratio in het oog met de laagste visus in de klinische groepen.

Concluderend kan gesteld worden dat crowding ratio's hoger zijn bij SZ kinderen dan bij GZ kinderen wanneer crowding gemeten wordt met een visuskaart met absolute spacing. Speciale klinische karakteristieken, zoals nystagmus en strabismus, hangen samen met sterkere crowdingeffecten.

## 2. Stimuluskarakteristieken

**Hoofdstuk 5** gaat in op de invloed van oculomotorische controle, crowding en aandachtsfactoren op visueel zoeken bij GZ kinderen (n = 11), SZ kinderen zonder nystagmus (n = 11) en SZ kinderen met nystagmus (n = 26). Drie zoektaken werden aan de kinderen gepresenteerd: (i) een rij met homogene *distractors*, (ii) een matrix met homogene *distractors*, en (iii) een matrix met heterogene *distractors*. Zoektaken met homogene distractors worden ook wel parallelle zoektaken genoemd, omdat veel informatie simultaan verwerkt kan worden. Zoektaken met heterogene distractors worden ook wel seriële zoektaken genoemd, omdat elementen afzonderlijk verwerkt moeten worden. Spacing werd gemanipuleerd in 5 stappen: 2', 4', 8', 16', en 32'. Symbolen werden aangeboden op 2× de grootte van het kleinst waarneembare optotype om zichtbaarheid te garanderen. Tijdens de simpele rij en matrix zoektaak

(homogene *distractors*) waren SZ kinderen met nystagmus minder accuraat dan GZ kinderen bij kleine spacing. Groepsverschillen namen toe bij de zoektaak met heterogene *distractors* (de seriële zoektaak). Zoektijden waren langer bij SZ kinderen dan GZ kinderen. De grotere verschillen tijdens de seriële zoektaak kunnen verklaard worden door de zwakkere oculomotorische controle van SZ kinderen met nystagmus.

## 2.1 Spacing

Zoals hierboven beschreven staat, zijn crowdingeffecten uiteraard sterker wanneer spacing kleiner is en wanneer er meer *distractors* om het doelobject staan (Hoofdstuk 2). Een andere stimuluseigenschap die crowding zou kunnen verklaren, is de configuratie van de stimulus. Ons onderzoek toont aan dat de invloed van spacing afhankelijk is van de stimulusconfiguratie. Bijvoorbeeld, wanneer GZ kinderen zoeken naar een uniek element in een rij met homogene *distractors* zal kleine spacing de zoektijd faciliteren (paragraaf 2.2.1). Echter, in een matrix configuratie zal kleine spacing de zoektijd niet faciliteren en de zoekprestatie zelfs ondermijnen (paragraaf 2.2.2).

## 2.2 Configuratie

### 2.2.1 Rij

De configuratie van een stimulus beïnvloedt het effect van element spacing. Tijdens het zoeken in een rij met homogene *distractors* (simpele zoektaak) zorgde kleine spacing niet altijd voor een verminderde prestatie. Kleine spacing in de rij faciliteerde het zoekproces juist bij GZ kinderen; hun zoektijden waren tot 40% korter voor trials met kleinere spacing. Deze laatste bevinding komt overeen met studies bij GZ volwassenen die aantonen dat patronen met dicht op elkaar geplaatste elementen makkelijker geïdentificeerd kunnen worden dan patronen met verder uit elkaar geplaatste elementen (Nothdurft, 1985, 1993; Scolari et al., 2007). Bij SZ kinderen was dit faciliterende effect afwezig.

### 2.2.2 Matrix

Tijdens simpele matrix zoektaken (met homogene *distractors*) heeft kleine spacing een negatieve impact op de prestatie. De SZ groep met nystagmus liet een lagere accuratesse zien bij 2' en 4' spacing dan GZ kinderen. Ten tweede zagen we dat deze negatieve invloed van kleine spacing op accuraatheid zich niet alleen uitte door verschil in accuratesse tussen GZ en SZ kinderen, maar we zagen ook dat er binnen beide groepen een effect was van spacing. Alle groepen waren trager bij kleinere spacing in een matrixconfiguratie. Tot slot zagen we dat SZ kinderen tot 5 keer trager waren dan GZ kinderen tijdens een simpele matrix zoektaak.



### 2.3 Distractor-distractor gelijkheid

Tijdens een complexe zoektaak in een matrix, een zoektaak met heterogene *distractors*, is de accuratesse van SZ kinderen met nystagmus lager in vergelijking met GZ kinderen tot de spacing groter was dan 16'. Dit geeft aan dat groepsverschillen groter zijn bij complexe zoektaken dan bij simpele zoektaken. Zoekprestatie is dus disproportioneel zwakker bij SZ kinderen dan GZ kinderen voor seriële zoektaken. Onze verklaring voor dit grotere groepsverschil tijdens seriële zoektaken in vergelijking met parallelle zoektaken is dat het niet per sé alleen de selectieve aandacht is die zwakker is, omdat groepsverschillen verdwenen bij de grootste spacing (32'). We denken dat oculomotorische controle een sleutelrol speelt tijdens zoektaken, omdat seriële zoektaken in grotere mate afhankelijk zijn van accurate oogbewegingen dan parallelle zoektaken (Young & Hulleman, 2013). We verwachten dat de zwakkere prestatie van SZ kinderen met nystagmus een resultaat is van het onvermogen om saccadegrootte aan te passen en stabiel te fixeren. GZ kinderen tonen een consistente aanpassing van de oogbewegingen aan stimulouseigenschappen, maar we zagen deze aanpassingen niet in dezelfde mate bij SZ kinderen. Om deze reden lijkt oculomotorische controle een voorwaarde om een seriële zoektaak met kleine, dicht op elkaar geplaatste symbolen uit te kunnen voeren.

### 2.4 Spacing en oogbewegingstrategie

Opnames van oogbewegingen laten twee groepsverschillen zien: (i) SZ kinderen met nystagmus maken meer fixaties dan GZ kinderen, en (ii) SZ kinderen met nystagmus maken grotere saccades dan GZ bij de kleinste spacing. De oogbewegingsstrategie die werd gevonden bij SZ kinderen met nystagmus wijkt af van de strategie die gevonden werd bij GZ kinderen en recente studies over oogbewegingen van GZ volwassenen (Vlaskamp & Hooge, 2006; Vlaskamp et al., 2005). De strategie die gezien werd bij SZ kinderen met nystagmus kan het beste worden verklaard door een grotere behoefte aan refixaties, omdat fixatieduur te kort is en een kind daardoor nog een keer het plaatje moet inspecteren. Meer refixaties (Kanonidou et al., 2010) en grotere saccade amplitudes (Shi et al., 2012) zijn ook gevonden bij volwassenen met amblyopie. Bij SZ kinderen zonder nystagmus werden geen verschillen gevonden ten opzichte van de overige twee groepen, maar dit kan (ten minste gedeeltelijk) gewijd worden aan de kleine groepsomvang van de kinderen met valide oogbewegingsopnames ( $n=4-6$ ).

De volgende stimulouseigenschappen zijn geassocieerd met crowding: (i) aantal *distractors*, (ii) stimulusconfiguratie, en (iii) de identiteit van de *distractors*. De aanwezigheid van nystagmus was wederom geassocieerd met sterkere crowdingeffecten.

### 3. Vergroting en crowding

In de dagelijkse praktijk wordt op scholen nog vaak gebruik gemaakt van uitvergrote kopieën van teksten om een SZ leerling toegang te geven tot lesmateriaal. Er zijn echter twee praktische voordelen verbonden aan het gebruik van een loep ten opzichte van uitvergrote print. Ten eerste biedt een loep kinderen de mogelijkheid om *elk* (type) materiaal te inspecteren, en ten tweede is een loep goedkoper dan het aanschaffen van boeken met uitvergrote tekst.

In **Hoofdstuk 4** werd de invloed van vergroting op crowding gemeten. SZ kinderen werden in twee groepen verdeeld (gematcht op leeftijd en nabijvisus): een loepgroep (4-6 jarigen [n = 13] en 7-8 jarigen [n = 19]), en een uitvergrote print groep (4-6 jarigen [n = 12] en 7-8 jarigen n=14). Als baseline werd de nabijvisus gemeten op 40 cm met absolute spacing. Daarna werd de nabijvisus nog een keer gemeten met vergroting. Prestatiematen die werden vergeleken waren: (i) de nabijvisus op 40 cm zonder vergroting, (ii) nabijvisus op 40 cm met vergroting, en (iii) de tijd om vijf optotypen te benoemen. Tijdens het werken met vergroting werd de werkafstand geregistreerd. Er was geen verschil in prestatie tussen de twee soorten vergroting voor de 4-6 jarigen en de 7-8 jarigen. De gemiddelde nabijvisus van de 4-6 jarige kinderen was 0.95 LogMAR zonder en 0.42 LogMAR met vergroting. De gemiddelde nabijvisus van de 7-8 jarige kinderen was 0.71 LogMAR zonder en 0.01 LogMAR met vergroting. Sterkere crowdingeffecten voorspelden grotere verbeteringen van de nabijvisus met vergroting.

De conclusie voortkomend uit het onderzoek is dat een loep en uitvergrote print even effectief zijn in het verbeteren van de prestatie van jonge kinderen met een brede visusrange op een crowded nabijvisus taak. Opvallend is dat kinderen met sterkere crowdingeffecten grotere vooruitgang boekten met uitvergroting. Dit kan gewijd worden aan de vergroting van de absolute spacing op de crowded nabijvisus taak. De kleine, absolute spacing van 2.6' op een niet-uitvergrote versie van de kaart is waarschijnlijk de bottleneck voor deze kinderen. Door middel van vergroting wordt op een kaart met absolute spacing deze bottleneck weggehaald. Acht kinderen (gemiddelde crowding ratio 1.9) lieten een grotere verbetering zien op de nabijvisus taak dan verwacht op basis van de totaal ontvangen uitvergroting (die teweeg werd gebracht door het verkorten van de kijkafstand en de loep of uitvergrote print). Voor deze kinderen moet de grotere absolute spacing die verkregen werd door vergroting aan te bieden de reden zijn geweest voor verbeterde prestatie. Bijvoorbeeld, een vergrotingsfactor van  $1.8\times$  vergroot de spacing op een kaart met absolute spacing van 2.6' naar 4.7'. Theoretisch valt het niet te verwachten dat een loep crowding

vermindert op kaarten met proportionele spacing, want op deze kaarten varieert spacing mee met de grootte van het optotype.

#### 4. Interventie op basis van perceptual learning

**Hoofdstuk 3** beschrijft de resultaten van literatuuronderzoek naar: (i) de mate van crowding in verschillende groepen (GZ kinderen, SZ kinderen en volwassenen, en kinderen met een cerebrale visuele beperking), en (ii) bestaande interventies voor het reduceren crowding. De meest effectieve interventie om crowding te verminderen lijkt Perceptual Learning (PL) te zijn. PL kan foveale crowdingeffecten verminderen bij volwassenen met amblyopie en in de normale periferie van GZ volwassenen. PL is gebaseerd op de notie dat het oefenen van een (in dit geval visuele) taak kan leiden tot een flinke en blijvende verbetering in het uitvoeren van deze taak (Huckauf & Nazir, 2007). De studies die zijn opgenomen in het literatuuronderzoek laten zien dat PL de kritische afstand, dat wil zeggen de minimale afstand die nodig is om objecten van elkaar te onderscheiden, kan verkleinen, de gezichtsscherpte kan verbeteren, contrastsensitiviteit kan verbeteren, oogstand kan verbeteren, en kan leiden tot een verbeterde efficiëntie van niet-retinotopie gebieden die geassocieerd worden met de hogere visuele informatieverwerking, zoals aandacht en besluitprocessen.

Gebaseerd op de kennis die verzameld is met behulp van onze onderzoeken en de onderzoeken van andere groepen werd een interventie ontwikkeld. Bepaalde stimulouseigenschappen spelen een cruciale rol in het uitlokken van crowding: spacing, stimulusconfiguratie (matrix), aantal *distractors*, en de *distractor-distractor* gelijkheid. Nystagmus en visuele aandacht bleken belangrijke persoonsgebonden factoren te zijn. Ons trainingsparadigma werd gebaseerd op deze factoren en bestond uit trainingsmateriaal met een kleine spacing, een matrix configuratie, een visuele zoekcomponent, en een ingebedde taakeis om het stimulusmateriaal element voor element te bekijken (daarmee deed de trainingstaak een beroep op het vermogen om kleine, precieze oogbewegingen te maken > ofwel het serieel kunnen zoeken).

**Hoofdstuk 7** toont aan dat de door ons ontwikkelde interventie op basis van PL effectief is in het verbeteren van de single en crowded nabijvisus en het verminderen van crowding in de helft van de SZ kinderen uit de crowded PL groep. Aan het interventieonderzoek hebben 45 SZ en 29 GZ kinderen deelgenomen. SZ kinderen werden in drie groepen verdeeld (gematcht op leeftijd en vertevisus): een loepgroep ( $n = 12$ ), een experimentele/crowded PL groep ( $n = 18$ ), en een controle/uncrowded PL groep ( $n = 15$ ). GZ kinderen werden ook in drie groepen verdeeld, maar werden alleen bij de voormeting gezien. Afhankelijke variabelen waren: single nabijvisus (single versie C-test met optotype spacing van ten minste  $30'$  of  $0.5^\circ$ ), crowded nabijvisus (i.e. leesvisus gemeten met crowded versie C-test met optotype afstand van  $2.6'$  of  $0.04^\circ$ ), LH 50% crowding nabijvisus, aantal opdrachten, accuraatheid,

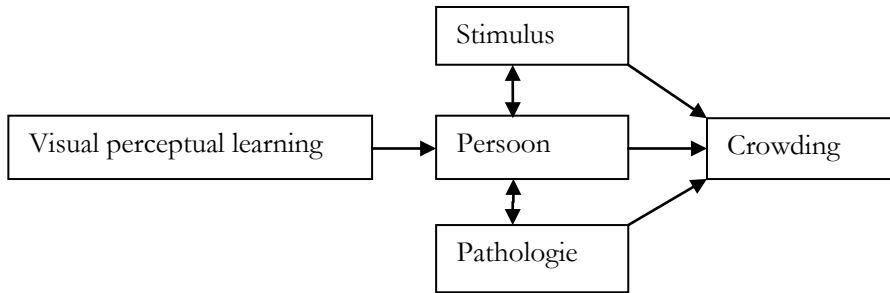
uitvoertijd, aantal kleine fouten en aantal grote fouten. SZ kinderen werden 6 weken getraind, 2× per week, 30 minuten (12 trainingssessies). Na training lieten kinderen een significante verbetering van de nabijvisus zien (1.3 LogMAR) en specifieke verbeteringen op de trainingstaak. De crowded PL groep liet de grootste verbetering in nabijvisus zien (1.7 LogMAR regels op de crowded visuskaart en lijkt daarmee de meeste geschikte training om de nabijvisus te verbeteren). Voor zover we weten, is dit de eerste interventiestudie die aantoont dat de nabijvisus van SZ kinderen significant verbetert na zes weken training.

Het doel van de interventie was om crowding te verminderen en de nabijvisus te verbeteren bij SZ kinderen. Vier belangrijke observaties werden gemaakt tijdens deze studie: (i) er waren baseline verschillen: SZ kinderen hadden wederom hogere crowding ratio's en maakten meer grote uitschieters tijdens de PL trainingstaak dan GZ kinderen (grote uitschieters zijn een indicatie voor vaker 'het spoor verliezen'), (ii) we vonden een verbetering van de single nabijvisus in alle trainingsgroepen (gemiddeld 1.3 LogMAR regels op de visuskaart), (iii) de crowded PL groep was de enige groep die een vooruitgang boekte op de crowded nabijvisus taak bij beide leeftijdscategorieën (4-6 en 7-9 jaar; zij gingen 1.7 LogMAR regels op de visuskaart vooruit), en (iv) we vonden geen significante afname van de crowding ratio in de trainingsgroepen. Er zijn indicaties dat SZ kinderen een tragere visuele rijping van hun single gezichtsscherpte laten zien dan GZ kinderen (zie Hoofdstuk 6). Deze tragere rijping zou een verklaring kunnen zijn voor het uitblijven van een reductie van de crowding ratio. Het valt te verwachten dat een verlengde trainingsperiode zou kunnen leiden tot grotere verbeteringen en een significante reductie van de crowding ratio. Deze vraag behoeft nader onderzoek.

### **Samengevat: training als compensatie voor verminderde visuele input**

In Figuur S.1.1 wordt een schematische weergave gegeven van onze belangrijkste bevindingen: een oogaandoening heeft een negatieve impact op de vroege stadia van de visuele informatieverwerking (zoals gezichtsscherpte; een maat die primair wordt bepaald door de kwaliteit van de informatie die vanaf de retina naar de visuele cortex wordt gestuurd), maar ook op latere stadia van de visuele informatieverwerking zoals foveale crowding, zoeksnelheid, en accuraatheid van zoeken in crowded displays (vaardigheden die in grotere mate afhankelijk zijn van extrastriate gebieden in het brein en aandacht).

Ons onderzoek toont aan dat er binnen de populatie van SZ kinderen bepaalde klinische factoren zijn die geassocieerd zijn met sterkere crowding: zoals de aanwezigheid van strabismus en nystagmus. Bij de meerderheid van de SZ kinderen is



**Figuur S.1.1** *Perceptual learning veroorzaakt directe specifieke leereffecten op een getrainde taak. Een indirect effect kan zijn dat gerelateerde vaardigheden (zoals visuele aandacht en oogmotoriek) voor een verbetering kunnen zorgen van de verwerking van het beeld, ook al is de input (het beeld) beschadigd door pathologie.*

er sprake van nystagmus en bovendien ligt de prevalentie van strabismus hoger bij SZ kinderen dan bij GZ kinderen. Deze factoren kunnen zorgen voor onderdrukking van visuele input (zoals bij amblyopie), of retinale beeldbeweging (in het geval van nystagmus) van binnenkomende visuele informatie, hetgeen dat leidt tot een verminderde spatiële resolutie (Chung & Bedell, 1995).

PL veroorzaakte een verbetering van de nabijvisus. Geen van de kindkarakteristieken (leeftijd, baseline nabijvisus, geslacht, locus van de pathologie (retinaal, iris, nystagmus of lens)), was gerelateerd aan de vooruitgang in nabijvisus die de kinderen lieten zien. We vermoeden dat de karakteristieken van het oog waarschijnlijk niet zijn veranderd na PL, maar dat de perceptuele en aandachtsnetwerken in het brein beiden worden beïnvloed door herhaaldelijke blootstelling aan kleine stimuli die om visuele aandachtfiltering vragen. Het onderzoek liet zien dat PL, zoals verwacht, directe specifieke leereffecten op de getrainde taak veroorzaakt, maar dat er daarnaast ook een indirect effect is op vaardigheden zoals visuele aandacht en fixatiestabiliteit. Juist het trainen van die vaardigheden lijkt te zorgen voor een gegeneraliseerd leereffect naar visuele functies die zijn aangedaan door pathologie. Deze training heeft dus een belangrijke meerwaarde voor de zorg aan slechtziende kinderen.

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