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Quantifying Visual Functions in Children with Cerebral Visual Impairment (CVI)

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Quantifying Visual Functions in Children with Cerebral Visual Impairment (CVI)

by

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Committee in charge:

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Abstract

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Patients with cerebral visual impairment (CVI, formerly cortical visual impairment) have vision loss resulting from an insult to the brain rather than to ocular structures. These children and their parents must attempt to understand their unique form of vision loss which often develops in an unpredictable fashion, and can go undiagnosed by an eye care provider. Furthermore, it can be difficult to advocate for children with CVI as many individuals and professionals who may interact with the child are unfamiliar with the condition. Although there is much interest in CVI as it is currently the leading cause of vision loss in children in the developed world, many aspects of vision loss in CVI are not well understood nor quantified.

The first two studies were aimed at understanding the effect of contour interaction on visual acuity in children with CVI. The first study shows a negative effect of contour interaction, the deleterious effect of identifying an object in the presence of other objects, on visual acuity in children with CVI as well as normally sighted children. This difference is more significant for children with CVI – and for this group, the greater the reduction of visual acuity, the greater the reduction in acuity with increased contour interaction. The second study shows that the critical spacing of this effect is about twice as large in children with CVI as compared to normally sighted children. The fifth study compared this effect in children with CVI to children with retinal disease. Surprisingly, there was minimal difference in the contour interaction effect between the two groups when looking at the average difference between measures. However, the slope of the trend was quite different for children with CVI versus children with retinal disease, implying that the underlying mechanism is quite different for the two groups. These two groups behave differently in the presence of contour interaction.

The third study involves comparing a commonly used pediatric visual acuity test, the Cardiff Acuity Test, to measuring vision with the same method used for the other studies - single Lea symbols surrounded by contour bars at half the optotype width away (50%) or the full optotype width away (100%). For 93% of the patients with CVI, 50% and 100% Lea symbols yielded a more reduced acuity compared to the Cardiff Acuity Test; the latter only requires

detection of the symbols, whereas the Lea symbols require discrimination between an apple and a house optotype.

Finally, the fourth study examined the relationship between contour interaction and contrast sensitivity in children with CVI. Preliminary findings show a positive correlation between contour interaction and contrast sensitivity. Understanding how object contrast affects contour interaction can be translated into real world recommendations for parents and teachers and can also serve as a basis for designing perceptual learning interventions.

The overarching goal of this research is to translate measurements into usable interventions to improve the lives of patients with CVI. In general, measuring visual acuity in children with CVI in the presence of contour interaction may give a better understanding of the child's visual potential and could be most useful when making recommendations to the child's family and care team.

Dumbledore watched her fly away, and as her silvery glow faded he turned back to Snape, and his eyes were full of tears.
"After all this time?"
"Always," said Snape.
J.K. Rowling, Harry Potter and the Deathly Hallows

To Joseph Davi: You, Me, Us - Always.

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Chapter 1

Background

Introduction

Parents of children with visual impairment have the challenging role of trying to understand their child's perception of the world, the capabilities of the child, and how he/she can function in the world. With ocular visual impairment, many visual functions are predictable based on the location of the physiological damage. However, patients with cerebral visual impairment (CVI, formerly cortical visual impairment) have vision loss resulting from an insult to the brain rather than to ocular structures. These children and their parents struggle to understand their unique form of vision loss which often develops in an unpredictable fashion, and can go undiagnosed by an eye care provider (Dutton, McKillop, and Saidkasimova 2006). Furthermore, it can be difficult to advocate for children with CVI as many individuals and professionals who may interact with the child are unfamiliar with the condition. Although there is much interest in CVI as it is currently the leading cause of vision loss in children in the developed world (Afshari, Afshari, and Fulton 2001), many aspects of vision loss in CVI are not well understood nor quantified. In this study, our goal is to quantify visual functions in children with CVI so that more accurate measurements can be taken in clinic and early interventions can be tested and developed.

Study Rationale

CVI continues to be an area of growing interest across multiple disciplines including neurobiology, optometry, ophthalmology, and education. CVI results from damage to the retrogeniculate visual pathway, specifically any region posterior to the lateral geniculate bodies. Hypoxic brain injury is the most common etiology of CVI (Afshari, Afshari, and Fulton 2001). Other common etiologies include prematurity, hydrocephalus, structural central nervous system abnormalities, and seizures (Khetpal and Donahue 2007).

The most common clinical finding of children with CVI is reduced visual acuity, followed by reduced contrast sensitivity and visual field defects (Fazzi et al. 2007). These deficits can

have a significant impact on an individual's ability to function effectively using their vision. To compensate for reduced acuity, the simplest way is to make the object of interest larger (in the clinic, this can be provided by using magnifiers) such that the size of the object exceeds the resolution limit. However, even when the object size is not a limiting factor, recognizing an object could be difficult if there are other objects in close proximity to the object of interest. This is the crowding effect and has been postulated as a major limiting factor for object recognition (Levi and Carney 2009; Pelli and Tillman 2008). Indeed, it has been shown that crowding affects many tasks of daily activities, including acuity (Flom, Weymouth, and Kahneman 1963), reading (Chung, Mansfield, and Legge 1998), face recognition (Whitney and Levi 2011), and reaching and grasping of objects (Bulakowski 2009), all of which have been reported to be difficult tasks for children with CVI (Zihl and Dutton 2015).To overcome the crowding effect, the object of interest must be separated from other objects by a sufficient distance. In the literature, this distance is referred to as the critical spacing. By definition, critical spacing refers to the minimum distance between an object of interest and its surrounding distractors (or, flankers). Parents of children with CVI often report that their child has difficulty locating objects when there is more than one object present. This is consistent with the crowding effect. Indeed, it has also been shown that children with CVI experience crowding that is up to three times greater than that experienced by adults (Huurneman et al. 2012). Based on the anecdotal reports of parents and the results of two related studies (Jacobson et al. 1996; Pike, Holmstrom, and Vries 1994), we hypothesize that children with CVI will have visual impairment from the effect of crowding.

Crowding refers to the deleterious effects of recognizing an object in the presence of other nearby objects. A closely related phenomenon, contour interaction, refers to a similar deleterious effect in recognizing a target as a result of nearby contours, such as bars. Flom suggested that crowding is the combined effects of contour interaction, attention, and eye movements (Flom 1991), although more recent studies seem to use these two terms interchangeably. Another commonly accepted distinction between crowding and contour interaction is that the flankers are often more complicated in the case of crowding and simpler, like bars, in the case of contour interaction. In the first chapter, we measured and quantified the magnitude and extent of the deleterious effect using visual acuity tests commonly used in the pediatric clinic - single Lea symbols with four surrounding bars to induce the deleterious effect. Therefore, the term contour interaction instead of crowding will be used throughout this dissertation.

We quantified the effect of contour interaction in children with CVI using high-contrast Lea symbols (black symbols printed on white cardboard). Details of the experimental approach are given in the next chapter. We measured visual acuity for symbols surrounded by four bars at several bar-to-symbol separations. This set of data tells us whether children with CVI show a decline in visual acuity with more contour interaction than age-matched normally sighted controls.

Children with CVI often exhibit a reduction in contrast sensitivity (Good, Hou, and Norcia

2012). Furthermore, contrast sensitivity is vital to functional vision and is often a better predictor of visual functions such as mobility (Marron and Bailey 1982) and face recognition (Owsley and Sloane 1987), as well as quality of life (Bansback et al. 2007). Studies in normally sighted individuals have shown that the crowding effect is reduced for low contrast letters as compared to high contrast letters when viewed with central fixation, that is, with the fovea (Kothe and Regan 1990). In addition, critical spacing has been shown to become smaller for low-contrast targets, more so in the periphery than in the fovea in normally sighted individuals (Coates, Chin, and Chung 2013). If these effects occur in children with CVI, then reducing the contrast of an object and its background may be a way to reduce crowding. However, reducing the contrast of objects may not be optimal given the contrast deficits of many children with CVI. We compared the threshold contrast sensitivity for detecting a grating target and the amount of contour interaction for visual acuity targets as a way to elucidate this relationship. Quantification of this finding in children with CVI may lead to a better understanding of functional vision in visual conditions of varying contrast which often more closely mimic real-world situations.

Public Health Impact

CVI is the leading cause of bilateral visual impairment in children in western countries (Good et al. 2001). According to the American Foundation for the Blind, 30-40% of cases of visual impairment in children is caused by CVI (Roman et al. 2008). Children born preterm or with low birth weight have a higher risk for visual impairment, including CVI (Vohr et al. 2000). According to the Centers for Disease Control and Prevention, the incidence of low birthweight and very low birthweight totals 9.4%. Additionally, the percent of children born preterm is 11.4% (Martin et al. 2015). Therefore, a large segment of the population could benefit from more accurate clinical measures and from information that could be used in early intervention services.

Definition of Cerebral Visual Impairment (CVI)

Cerebral visual impairment (CVI, also known as cortical visual impairment) is the leading cause of childhood vision loss in developed nations and results from an insult to the developing brain. That is, it is a reduction in visual acuity and other visual functions caused by damage to the visual pathway, rather than to the ocular structures. It should be noted that although CVI may be present and sufficient to cause vision loss on its own, there are often associated ocular conditions such as optic nerve atrophy, optic nerve hypoplasia, and retinopathy of prematurity, as well as associated systemic conditions such as cerebral palsy and epilepsy.

Associated Ocular Etiologies

Optic nerve atrophy can be seen in the presence of CVI due to retrograde degeneration from the brain to the optic nerve. When a nerve axon is damaged in any way, the remaining section connected to the neuronal cell body undergoes damage which causes degeneration of the tissue. As a result, children with CVI may be born with normally appearing optic nerves that may look pale and degenerative after a few years of life.

Optic nerve hypoplasia is commonly found concurrently in children with CVI. The cause is typically idiopathic; there is an association with optic nerve hypoplasia and first born children of young mothers. There is also an increased risk in mothers with diabetes. Optic nerve hypoplasia occurs secondary to retinal ganglion cell axon degeneration, specifically when central connections are disrupted. This degeneration of axons occurs as part of normal visual pathway development. However, in the case of optic nerve hypoplasia, the process is carried out excessively, resulting in fewer axons and small hypoplastic nerves (Borchert et al. 1995).

Septo-optic dysplasia is another commonly found condition in the presence of CVI and is related to optic nerve hypoplasia. It typically manifests as midline abnormalities of the brain including absence of the septum pellucidum and agenesis of the corpus callosum. It can also cause dysplasia of the third ventricle. These brain abnormalities are commonly associated with optic nerve hypoplasia. Another characteristic finding in septo-optic dysplasia is a deficiency of growth hormone. Other hormonal abnormalities include hypothyroidism, neonatal hypoglycemia, hypadrenalism, and diabetes insipidus. As a result of hormonal imbalances, children with septo-optic dysplasia may be classified as having failure to thrive (Izenberg, Rosenblum, and Parks 1984).

CVI is commonly found in children who are born prematurely. As a result, retinopathy of prematurity (ROP) is often an associated finding. It most commonly affects infants weighing 1250 grams (2.75 pounds) or less, especially those born before 31 weeks gestation. Low birth weight is the major risk factor in the development of ROP. According to the National Eye Institute (NEI), 3.9 million infants are born in the United States each year. Of those, about 28,000 weigh 1250 grams or less. About half of those babies are affected by some level of ROP, although only 10% require some amount of medical treatment.

ROP can be classified into five stages. Stage I involves mildly abnormal blood vessel growth. At this stage, the disease typically resolves without treatment. Stage II findings include a moderate level of blood vessel growth, however, even in light of moderate growth, many children still develop normal vision. Stage III is classified as severely abnormal blood vessel growth - often if the blood vessels appear twisted and enlarged this would encourage treatment to prevent retinal detachment. Stage IV involves a tractional retinal detachment (partial); this traction causes a pulling of the retinal tissue away from the wall of the eye. In Stage IV, the most severe stage, a completely detached retina is seen and can result in

severe visual impairment and blindness if untreated (An International Committee for the Classification of Retinopathy of Prematurity 2005).

Incidence

CVI is the most common cause of visual impairment in children (Matsuba and Jan 2006), whereas in the past, inherited congenital ocular disease and disorders predominated. Studies cite this increase in cases of CVI to be due to advances in neonatal care (Lambert et al. 1987; Good et al. 1994). Further increases are thought to be due to successful management of childhood blindness resulting from cataract and retinopathy of prematurity (Philip and Dutton 2014). In children under 16 years of age, visual impairment occurs in about 10-22 per 10,000 births in developed countries. In developing countries, the number is closer to 40 per 10,000 births (Gilbert et al. 1999). It is expected that these numbers would be even higher if there were more widespread identification of perceptual (or functional) visual impairment (Williams et al. 2011; Macintyre-Bon et al. 2013).

Etiologies

The most common etiology of CVI is perinatal or neonatal hypoxic ischemic encephalopathy (HIE) (Matsuba and Jan 2006). Other complications which can cause perinatal hypoxia can also lead to CVI and include cardiac arrest, umbilical cord entanglement, and placental abruption or insufficiency. Infection, hydrocephalus, and metabolic disorders can also cause CVI (Watson 2008).

Associated Conditions

Non-ambulatory cerebral palsy is highly associated with CVI and has been found to be as high as 70%. Sensorineural hearing loss is also common in the presence of CVI. (Matsuba and Jan 2006). Motor and cognitive disabilities can be found depending on the specific etiology of CVI. Aside from cerebral palsy, cognitive impairment and seizures are also commonly found (Watson 2008).

Optic nerve atrophy and optic nerve hypoplasia are commonly associated with CVI (Good et al. 1987). Nystagmus is also a common finding, although it is not typically present if there is only cortical insult, but rather if there are associated ocular findings present as well (Good et al. 1994).

Prognosis

In general, children with CVI have a tendency toward improved visual outcome over time (Matsuba and Jan 2006). Children with CVI who have better visual acuity levels over time tend to have better motor and cognitive outcomes (Matsuba and Jan 2006). Although there

is typically an improvement in vision over time, most patients with CVI will not regain completely normal vision (Good et al. 2001). The prognosis is also dependent on the severity and location of the brain damage. For example, damage that occurs in the striate cortex rather than the optic radiations may have a better chance of recovering, whereas basal ganglia involvement usually indicates a poor outcome (Lambert et al. 2015; Mercuri et al. 1997). The poorest prognosis is found in the presence of bacterial meningitis, cardiac arrest, and status epilepticus (epileptic seizures that occur continuously without regaining consciousness) (Wong 1991). Children diagnosed before age three tend to have a greater level of visual improvement (Huo et al. 1999).

Clinical Presentations of CVI

As previously discussed, the clinical presentation of CVI is dependent upon the location, extent, and timing of the damage which occurs. However, various studies have characterized the types of clinical presentations that are often detected in children with CVI. Table 1.1 gives specific examples (non-exhaustive) of the types of issues that are often noticed when a child presents for a clinical visit.

Reductions in Visual Functions

Visual Acuity

Visual dysfunction in CVI can present in a number of ways. However, visual acuity is often reduced to varying degrees, and this can occur in the presence of normal pupil responses and ocular structures which also appear normal upon examination (McKillop and Dutton 2008). It is important to collect visual acuity measurements on children with CVI, and it is often preferred to utilize more than one method. The two major clinical techniques for measuring visual acuity in pediatric populations include forced-choice preferential looking (PL) and the Visual Evoked Potential (VEP) (see discussion of PL and VEP below). Visual acuity measurements vary depending on the acuity target, and much care must be given not to overestimate a child's visual abilities since they may be deemed ineligible for vision impairment or low vision services. Furthermore, visual acuity is not the only important factor when assessing visual function. In fact, other aspects of visual function may play an even greater role in day to day tasks rather than high-contrast visual acuity as typically measured in an eye examination.

Contrast Sensitivity

Contrast sensitivity can be described as an observer's ability to detect subtle shades of grey or brightness differences from the background. Contrast sensitivity can be a useful measure of visual function, as it translates well to functionality in day to day life (seeing

Reported Behavior	References
Reduction in acuity	Philip & Dutton 2014
Light gazing	Jan et al. 1990
Photophobia	Jan, Groenveld, Anderson 1993
Poor visual attention	Jan et al. 1987
Color preference	Roman-Lantzy 2007
Restricted visual fields	Philip & Dutton 2014
Difficulties with complex visual patterns	Dutton et al. 2006, Roman-Lantzy 2007
Difficulties finding an object at a distance	Dutton et al. 2006, Roman-Lantzy 2007
Better recognition of familiar objects than novel ones	Roman-Lantzy 2007
Looking away when reaching	Good 2001, Roman-Lantzy 2007
Visual latency	Roman-Lantzy, 2007
Variability in contrast	Good 2001

Table 1.1: Reported Clinical Behaviors in CVI.

curbs/stairs/changes in elevation, detecting objects, recognizing borders). Contrast sensitivity has the potential to be significantly reduced in children with CVI, although this is not always the case (McKillop and Dutton 2008). Premature children may be more likely to have reductions in contrast sensitivity, due to earlier development of the magnocellular as compared to the parvocellular pathways (Bosworth and Dobkins 2013; Bosworth et al. 2013).

Visual Fields

As expected, there is a specific pattern to visual field defects in the presence of brain damage that is directly related to the site of damage. In CVI, if there is damage to the occipital lobes, visual field loss typically occurs to the side opposite the damage (Philip and Dutton 2014). Damage to the parietal lobe also creates lack of attention on the side opposite the damage. In premature children, damage often occurs in the periventricular white matter, which causes lower visual field impairment (Jacobson, Flodmark, and Martin 2006). Furthermore, it is important to note that attention can play a large role when assessing visual fields. Children with CVI will often become fixated on a particular object and may ignore their surroundings simply for attentional reasons rather than a truly organic visual field deficit.

Color Vision

Color vision in children with CVI appears to be normal overall, although low contrast color differences may be challenging if contrast sensitivity is also reduced. As compared to other visual functions, color vision has not been studied extensively. It is worth mentioning that, as a general rule, most subjects in the CVI population included in the following studies did not exhibit difficulties with color discrimination.

Crowding and Contour Interaction

Crowding is defined as the deleterious effect of nearby contours on visual discrimination. One of the original groundbreaking ideas about crowding comes from Flom, Heath, and Takahashi (1963) when they found that crowding occurs even if the target and flanker are presented to different eyes. This finding suggests that crowding maps to a cortical locus. In 1970, Bouma made his famous discovery that the extent of crowding is a constant fraction of the target eccentricity, and this is now called Bouma's constant. More recent work has shown that there is likely an attentional filter that functions to limit the amount of visual information that is consciously available; this is validated by the finding that adaptation to an orientation-specific target is not affected by crowding (He, Cavanagh, Intrilligator 1996).

In the fovea, crowding is thought to occur over a small distance of 4-6 arcmin. In the periphery, it is thought to occur up to 0.5 times the eccentricity of the target (Bouma's constant). Furthermore, crowding has been shown to occur in a variety of tasks including letter recognition (Bouma 1970), Vernier acuity (Westheimer and Hauske 1975), orientation discrimination (Andriessen and Bouma 1976), stereoacuity (Butler and Westheimer 1978), and face recognition (Martelli, Majaj, and Pelli 2005). Crowding is not simply a property of luminance channels, as shown by Tripathy and Cavanagh (2002) which furthers the argument for an attentional model for crowding (Tripathy and Cavanagh 2002). Crowding has been shown to occur for moving stimuli and is relatively independent of the speed of motion (Bex, Dakin, and Simmers 2003).

Methodology: Forced Choice Preferential Looking (PL)

From 1975 to 1985, an important method emerged in the field of infant vision known as preferential looking (Fantz 1965). Infants preferred to fixate complex visual targets for longer periods of time compared to their fixation on less complex or homogenous fields. In 1974, Teller et al. built on this concept and added a forced choice paradigm (choice between two alternatives) where an observer, unaware of the location of the visual target, had to choose its location based on their observation of an infant's fixation, i.e. forced choice preferential looking (Teller et al. 1974). Others took this methodology and combined it with visual psychophysics (Atkinson, Braddick, and Braddick 1974). A significant improvement was made

in this period of great interest in infant vision that drastically changed the existing approach to visual acuity measurements. Teller et al. developed the acuity card procedure - a simplified method of measuring visual acuity in infants and young children (Teller et al. 1986). Building on the work of others, (Dubowitz 1980), (Dubowitz, Morante, and Verghote 1980) and (Morante et al. 1982), they were able to demonstrate a new fast and accurate method of obtaining visual acuity in populations that may otherwise be challenging to assess, and they found that the results translated well across clinical and laboratory settings alike. The procedure involves presentation of a series of cards with gratings (black and white stripes) of different spatial frequencies on a grey background to a child by an adult observer. The observer uses numerous pieces of information including fixation, eye movements, pointing, and head movement, and observes the child's looking behavior through a peephole in the cards. This continues until there is a clear indication as to the finest grating observed by the child. This can be applied to other preferential looking procedures with other stimulus types as well.

A debate continued throughout this period comparing the difference in accuracy of visual measurements taken with preferential looking versus a form of objective measurement such as the visual evoked potential (VEP). The discrepancies between behavioral and objective methods of visual acuity measurement have long been contested. Numerous groups have argued for why one method should be used over the other in various pediatric groups. Visual evoked potential (VEP) has been argued to be a reliable method of measuring vision in children with CVI (Good 2001). On the other hand, one study in 42 children with moderate to severe visual impairment found better accuracy with preferential looking (PL) as compared to VEP (Bane and Birch 1992). Still others compared PL and VEP in children with CVI; they found an improvement in visual acuity for both methods on subsequent visits. In some individuals, large disparities were found between preferential looking and VEP visual acuity (Lim et al. 2005).

Watson et al. analyzed the relationship between early objective measurements of visual acuity with the VEP and how this compared to future behavioral measurements of visual acuity with preferential looking. They found that the initial VEP measure was much better than the initial behavioral measurement, and furthermore, the early VEP measurement corresponded well with the behavioral acuity measured approximately seven years later (Watson, Orel-Bixler, and Haegerström-Portnoy 2010).

References

1. Afshari, Mehran A., Nasrin A. Afshari, and Anne B. Fulton. 2001. Cortical Visual Impairment in Infants and Children. International Ophthalmology Clinics 41 (1): 159-69.

2. Andriessen, J.J., and H. Bouma. 1976. Eccentric Vision: Adverse Interactions between

Line Segments. Vision Research 16 (1): 71-78.

3. Bansback, N., C. Czoski-Murray, J. Carlton, G. Lewis, L. Hughes, M. Espallargues, C. Brand, and J. Brazier. 2007. Determinants of Health Related Quality of Life and Health State Utility in Patients with Age Related Macular Degeneration: The Association of Contrast Sensitivity and Visual Acuity. Quality of Life Research 16 (3): 533-43.

4. Bex, Peter J., Steven C. Dakin, and Anita J. Simmers. 2003. The Shape and Size of Crowding for Moving Targets. Vision Research 43 (27): 2895-2904.

5. Borchert, M., D. McCulloch, C. Rother, and A. U. Stout. 1995. Clinical Assessment, Optic Disk Measurements, and Visual-Evoked Potential in Optic Nerve Hypoplasia. American Journal of Ophthalmology 120 (5): 60512.

6. Bosworth, Rain, and Karen Dobkins. 2013. Effects of Prematurity on the Development of Contrast Sensitivity: Testing the Visual Experience Hypothesis. Vision Research 82: 31-41.

7. Bosworth, Rain, Shira L. Robbins, David B. Granet, and Karen Dobkins. 2013. Delayed Luminance and Chromatic Contrast Sensitivity in Infants with Spontaneously Regressed Retinopathy of Prematurity Rain. Documenta Ophthalmologica 127 (1): 57-68.

8. Bouma, H. 1970. Interaction Effects in Parafoveal Letter Recognition. Nature 226: 17778.

9. Bulakowski, Paul. 2009. Visuomotor Crowding: The Resolution of Grasping in Cluttered Scenes. Frontiers in Behavioral Neuroscience 3 (November): 1-7.

10. Butler, T W, and G Westheimer. 1978. Interference with Stereoscopic Acuity: Spatial, Temporal, and Disparity Tuning. Vision Research 18 (10): 1387-92.

11. Chung, Susana T.L., J.Stephen Mansfield, and Gordon E. Legge. 1998. Psychophysics of Reading. XVIII. The Effect of Print Size on Reading Speed in Normal Peripheral Vision. Vision Research 38 (19): 2949-62.

12. Coates, Daniel Robert, Jeremy M Chin, and Susana T.L. Chung. 2013. Factors Affecting Crowded Acuity: Eccentricity and Contrast. Optometry Vision Science 90 (7): 996-1005.

13. Dutton, G N, E C A McKillop, and S Saidkasimova. 2006. Visual Problems as a Result of Brain Damage in Children. The British Journal of Ophthalmology 90 (8): 932-33.

14. Fazzi, Elisa, Sabrina Giovanna Signorini, Stefania Maria Bova, Roberta La Piana, Paola Ondei, Chiara Bertone, Walter Misefari, and Paolo Emilio Bianchi. 2007. Spectrum of Visual Disorders in Children with Cerebral Visual Impairment. Journal of Child Neurology 22 (3): 294-301.

15. Flom, Mert. 1991. Contour Interaction and the Crowding Effect. Problems in Optometry 3 (2): 237-57.

16. Flom, Mert, Frank W Weymouth, and Daniel Kahneman. 1963. Visual Resolution and Contour Interaction. Journal of the Optical Society of America 53 (9): 1026-32.

17. Gilbert, C.E., L. Anderton, L. Dandona, and A. Foster. 1999. Prevalence of Visual Impairment in Children: A Review of Available Data. Ophthalmic Epidemiology 6 (1): 73-82.

18. Good, William V., C. Hou, and A. Norcia. 2012. Spatial Contrast Sensitivity Vision Loss In Children With Cortical Visual Impairment. Investigative Ophthalmology Visual Science 53 (12): 7730-34.

19. Good, William V., J. Jan, S. Burden, A. Skoczenski, and T Rowan Candy. 2001. Recent Advances in Cortical Visual Impairment. Developmental Medicine and Child Neurology 43: 56-60.

20. Huo, R, S K Burden, C S Hoyt, and W V Good. 1999. Chronic Cortical Visual Impairment in Children: Aetiology, Prognosis, and Associated Neurological Deficits. Br J Ophthalmol 83 (6): 670-75.

21. Huurneman, Bianca, F Nienke Boonstra, Ralf Fa Cox, Antonius Hc Cillessen, and Ger Van Rens. 2012. A Systematic Review on 'Foveal Crowding 'in Visually Impaired Children and Perceptual Learning as a Method to Reduce Crowding. BMC Ophthalmology 12(27).

22. An International Committee for the Classification of Retinopathy of Prematurity. 2005. The International Classification of Retinopathy of Prematurity Revisited. Archives of Ophthalmology 123 (7): 991.

23. Izenberg, Neil, Mindy Rosenblum, and John S Parks. 1984. The Endocrine Spectrum of Septo-Optic Dysplasia. Clinical Pediatrics 23 (11): 632-36.

24. Jacobson, L, U Ek, E Fernell, O Flodmark, and U Broberger. 1996. Visual Impairment in Preterm Children with Periventricular Leukomalacia–Visual, Cognitive and Neuropaediatric Characteristics Related to Cerebral Imaging. Developmental Medicine and Child Neurology 38: 724-35.

25. Jacobson, Lena, Olof Flodmark, and Lene Martin. 2006. Visual Field Defects in Prematurely Born Patients with White Matter Damage of Immaturity: A Multiple-Case Study. Acta Ophthalmologica Scandinavica 84 (3): 357-62.

26. Khetpal, Vijay, and Sean P. Donahue. 2007. Cortical Visual Impairment: Etiology, Associated Findings, and Prognosis in a Tertiary Care Setting. Journal of American Association for Pediatric Ophthalmology and Strabismus 11 (3): 235-39.

27. Kothe, Angela C., and David Regan. 1990. Crowding Depends on Contrast. Optometry Vision Science 67 (4): 283-86.

28. Lambert, Scott R, Creig S Hoyt, James E Jan, James Barkovich, and Olof Flodmark. 2015. Computed Tomographic and Magnetic Resonance Imaging Predictors.

29. Levi, Dennis M, and Thom Carney. 2009. Crowding in Peripheral Vision: Why Bigger Is Better. Current Biology: CB 19 (23): 1988-93.

30. Macintyre-Bon, Catriona, David Young, Gordon N. Dutton, Kate Mitchell, Judith Simpson, Gunter Loffler, Richard Bowman, and Ruth Hamilton. 2013. Cerebral Visual Dysfunction in Prematurely Born Children Attending Mainstream School. Documenta Ophthalmologica 127 (2): 89-102.

31. Marron, J A, and I L Bailey. 1982. Visual Factors and Orientation-Mobility Performance. American Journal of Optometry and Physiological Optics 59 (5): 413-26.

32. Martelli, Marialuisa, Najib J. Majaj, and Denis G. Pelli. 2005. Are Faces Processed like Words? A Diagnostic Test for Recognition by Parts. Journal of Vision 5 (1): 6.

33. Martin, Joyce A, Brady E Hamilton, D Ph, Michelle J K Osterman, Sally C Curtin, and T J Mathews. 2015. National Vital Statistics Reports. Vol. 64.

34. McKillop, Elisabeth, and Gordon N Dutton. 2008. Impairment of Vision in Children Due to Damage to the Brain: A Practical Approach. Br. Ir. Orthopt. J. 65 (003): 8-14.

35. Mercuri, E., Janette Atkinson, O. Braddick, Shirley Anker, Frances Cowan, Mary Rutherford, Jackie Pennock, and Lilly Dubowitz. 1997. Visual Function in Full-Term Infants with Hypoxic-Ischaemic Encephalopathy. Neuropediatrics 28 (03). Hippokrates Verlag GmbH Stuttgart: 155-61.

36. Owsley, C, and M E Sloane. 1987. Contrast Sensitivity, Acuity, and the Perception of 'real-World 'Targets. British Journal of Ophthalmology 71 (10): 791-96.

37. Pelli, Denis G, and Katharine A Tillman. 2008. The Uncrowded Window of Object Recognition. Nature Neuroscience 11 (10): 1129-35.

38. Philip, Swetha Sara, and Gordon N Dutton. 2014. Identifying and Characterising Cerebral Visual Impairment in Children: A Review. Clinical and Experimental Optometry 97 (3): 196-208.

39. Pike, MG, G Holmstrom, and LS De Vries. 1994. Patterns of Visual Impairment Associated with Lesions of the Preterm Infant Brain. Developmental Medicine and Child Neurology 36: 849-62.

40. Roman, C., L. Baker-Nobles, G. Dutton, T. Luiselli, B. Flener, J. Jan, A. Lantzy, et al. 2008. Statement on Cortical Visual Impairment. American Foundation for the Blind. 2008.

41. Tripathy, Srimant P., and Patrick Cavanagh. 2002. The Extent of Crowding in Peripheral Vision Does Not Scale with Target Size. Vision Research 42 (20): 2357-69.

42. Vohr, B R, L L Wright, a M Dusick, L Mele, J Verter, J J Steichen, N P Simon, et al. 2000. Neurodevelopmental and Functional Outcomes of Extremely Low Birth Weight Infants in the National Institute of Child Health and Human Development Neonatal Research Network, 1993-1994. Pediatrics 105 (6): 1216-26.

43. Watson, Tonya Ann. 2008. Quantitative Assessment of Vision Function in Children with Cortical Visual Impairment.

44. Westheimer, G, and G Hauske. 1975. Temporal and Spatial Interference with Vernier Acuity. Vision Research 15 (October): 1137-41.

45. Whitney, David, and Dennis M Levi. 2011. Visual Crowding: A Fundamental Limit on Conscious Perception and Object Recognition. Trends in Cognitive Sciences 15 (4): 160-68.

46. Williams, Cathy, Kate Northstone, Ricardo Sabates, Leon Feinstein, Alan Emond, and Gordon N. Dutton. 2011. Visual Perceptual Difficulties and Under-Achievement at School in a Large Community-Based Sample of Children. PLoS ONE 6 (3).

47. Wong, Virginia C.N. 1991. Cortical Blindness in Children: A Study of Etiology and Prognosis. Pediatric Neurology 7 (3): 178-85.

48. Zihl, Josef, and Gordon N Dutton. 2015. Cerebral Visual Impairment in Children.

Chapter 2

Contour interaction

Background

Defining Cerebral Visual Impairment (CVI)

As discussed in the background chapter, cerebral visual impairment (CVI) is the leading cause of vision loss in children in industrialized nations and results from an insult to the developing brain. Anecdotal reports indicate that children with CVI may have more difficulty with identifying symbols in the presence of crowding and surrounding contours. The goal of this study was to compare the level of visual acuity reduction that may occur in the presence of contour interaction.

History of Research in Children's Vision

In 1963, Wiesel and Hubel famously introduced the concept that there is plasticity of the visual cortical organization in animals (Wiesel and Hubel 1963). This laid important ground work for the concept that the development of infant visual capabilities could be understood through structural and functional development of the visual system.

From 1975 to 1985, there was a period of rapid growth in researching the development of visual acuity, contrast sensitivity, refraction, and accommodation in human infants. The development of clinical methods that could better measure visual functions in infants and young children was a driving force. One important finding was the observation that infants prefer to fixate complex visual targets over homogenous grey fields (Fantz 1965). In 1974, Teller et al. built on this concept and added a forced choice paradigm (choice between two alternatives) where an observer, unaware of the location of the visual target, had to choose its location based on their observation of an infant's fixation, i.e. forced choice preferential looking (Teller et al. 1974). Others took this methodology and combined it with visual psychophysics (Atkinson, Braddick, and Braddick 1974).

By 1980, there was a clear picture of how visual acuity develops rapidly in the first months of life, although there was still some debate between behavioral based and objective based visual evoked potential (VEP) brain wave measures. This research brought up another question: what limits visual acuity and contrast sensitivity in infants? The role of visual optics and accommodation was examined through measurements of refractive error in infants using dynamic and near retinoscopy (Banks 1980; Mohindra 1977; Gwiazda et al. 1978), new methods of photorefraction where a modified camera produced images that, after interpretation, could screen for refractive errors (Howland et al. 1978; Braddick et al. 1979; Hainline et al. 1992), and large scale refractive screening of infants (Howland et al. 1978; Braddick et al. 1979; Hainline et al. 1992).

A more interesting potential limit is imposed by the immature outer segment morphology and packing density of the foveal cones, as well as small eye diameter in newborn infants (Yuodelis and Hendrickson 1986). Banks and Bennett (1988) calculated what would be the effect of these immaturities if the infant visual system then uses the information supplied by the cones as efficiently as the adult visual system. The calculation suggests that if the improvement of acuity from one month of age to adult is taken as 12-fold, only about 25% of this change can be attributed to the photoreceptors and to increasing eye size (Banks and Bennett 1988).

Ultimately, cortical magnification has been shown consistently to correlate with and to limit visual acuity. For example, Vernier acuity has been shown to be limited by cortical magnification in V1 (Duncan and Boynton 2010). Additionally, higher level visual processes such as crowding have been demonstrated to occur at multiple stages in the visual hierarchy (Whitney and Levi 2011a).

Modified Acuity Card Procedure

An important piece of methodology emerged in this period of great interest in infant vision that drastically changed the existing approach to visual acuity measurements. Teller et al. developed the acuity card procedure - a simplified method of measuring visual acuity in infants and young children (Teller et al. 1986). Building on the work of others, (Dubowitz 1980; Dubowitz, Morante, and Verghote 1980; Morante et al. 1982), they were able to demonstrate a new fast and accurate method of obtaining visual acuity in populations that may otherwise be challenging to assess, and they found that the results translated well across clinical and laboratory settings alike. The procedure involves presentation of a grating card to a child by an adult observer. The grating card is a large card with a square wave grating on one side and a uniform blank grey field on the other side. The observer uses numerous pieces of information including fixation, eye movements, pointing, and head movement and observes the child's looking behavior through a peephole in the cards. This continues until there is a clear indication as to the finest grating observed by the child. This can be applied to other preferential looking procedures with other stimulus types as well.

Behavioral and Objective Measurements of Visual Acuity

Grating acuity does not always correlate with optotype acuity (Dobson et al. 1999). Grating acuity may simply be a measure of pattern resolution rather than discrimination, as is required with optotype acuity. As a result, grating acuity is limited in its ability to always provide accurate measurements of visual functions and abilities.

The discrepancies between behavioral and objective methods of visual acuity measurement have long been contested. Numerous groups have argued for why one method should be used over the other in various pediatric groups. Visual evoked potential (VEP) has been argued to be a reliable method of measuring vision in children with CVI (Good 2001). On the other hand, one study in 42 children with moderate to severe visual impairment found better accuracy with preferential looking (PL) as compared to VEP (Bane and Birch 1992). Still others compared PL and VEP in children with CVI; they found an improvement in visual acuity for both methods on subsequent visits. In some individuals, large disparities were found between preferential looking and VEP visual acuity (Lim et al. 2005).

Watson et al. analyzed the relationship between early objective measurements of visual acuity with the VEP and how this compared to future behavioral measurements of visual acuity with preferential looking in children with CVI. They found that the initial VEP measure was much better than the initial behavioral measurement, and furthermore, the early VEP measurement corresponded well with the behavioral acuity measured approximately seven years later (Watson, Orel-Bixler, and Haegerström-Portnoy 2010).

Contour Interaction

Contour interaction is a well-established concept in vision science literature. It is the phenomenon by which letter recognition is degraded by the presence of neighboring contours. The effect is largest when a target is presented in the retinal periphery. In populations such as individuals with amblyopia, this phenomenon may occur in the amblyopic eye at central fixation. Contour interaction has been extensively studied on a number of parameters, especially when varying the target and flanker. Orientation of target and flankers affects sensitivity, especially when the two are more similar (Andriessen and Bouma 1976). Similarity between target and background also decreases letter recognition (Estes 1982; Nazir 1992), and there is a stronger contour interaction effect if the target and flanker are more similar (Kooi et al. 1994; Andriessen and Bouma 1976; Estes 1982; Nazir 1992; Polat and Sagi 1993). Some individuals showed significant improvement in tasks when target and flankers were different colors, but this effect did not hold for all individuals studied. Presenting a different polarity (black versus white) of target and flankers causes the effect of contour interaction to decrease. The effect of flankers depends on both the strength of the flankers relative to the target and the degree of similarity. A greater difference in depth (stereopsis) between the two eyes also decreases interactions. There is no significant effect on the rela-

tive difficulty of detecting targets with neither similar nor dissimilar distractors (Kooi et al. 1994). The eye of origin (the eye viewing either target or flanker) was found not to matter with respect to the interaction, both foveally (Flom, Heath, and Takahashi 1963), and in the periphery (Kooi et al. 1994). The probability of detecting an embedded target increases as the target and background become less similar (Kröse 1987; Duncan and Humphreys 1989). Many researchers believe this to be dependent on the pop-out effect which is that a target will be more likely to stand out if it is considerably different from its surrounding flankers along various parameters because it is perceptually separable from its surroundings (Treisman and Souther 1985).

There are two major models utilized to discuss contour interaction or feature interaction. One model describes how two nearby items compete for a limited set of feature detectors (Estes 1972). These feature detectors transform the incoming information and make comparisons. One area of uncertainty within this model is whether there are interactions between specific channels (routes by which information is transmitted) or if they operate independently from their neighboring channels. In earlier work, Estes determined that there are mutual inhibitory interactions which increase from central toward peripheral locations in the visual field. Shiffrin and Gardner elaborated further upon this idea but proposed an independent channels model (Shiffrin and Gardner 1972). Later work by Egeth concluded that independent channels are well supported for certain circumstances but not for others (Egeth 1977).

The second model posits that features of a character or visual target drift over time. This work demonstrated that several processes contribute including response competition, distribution of attention, perceptual grouping, and contour interaction. Contour interaction was found to dominate at close spacing, but the other processes were found to dominate when the spacing was wider (Wolford and Chambers 1983).

In normally sighted individuals, contour interaction occurs over a smaller range at the fovea compared to retinal eccentricities beyond the fovea (Bouma 1970; Toet and Levi 1992; Kooi et al. 1994). Foveal contour interaction is thought to occur over 4-6 arcmin (Flom, Weymouth, and Kahneman 1963); furthermore, there is a small range of target sizes in which flankers result in genuine foveal crowding. If targets are larger, this results in masking rather than contour interaction. Visual masking is used to describe the phenomenon by which a pattern can reduce the detectability or discriminability of a target. It typically occurs for targets and masks that overlap in visual space, and the phenomenon and mechanisms are reasonably well understood. At the fovea, the extent of contour interaction depends on the size of the optotypes used (Ehrt and Hess 2005), and the extent of contour interaction is proportional to stimulus size (Levi, Hariharan, and Klein 2002; Tripathy and Cavanagh 2002; Pelli et al. 2007; Pelli, Palomares, and Majaj 2004). The strength and extent of peripheral contour interaction is much greater than masking, and therefore the interactions that affect visual acuity cannot simply be attributed to masking (Andriessen and Bouma 1976; Levi, Hariharan, and Klein 2002). Unlike in the periphery, foveal contour interaction cannot

be easily distinguished from masking. The fovea depends primarily on contour interaction, whereas eccentric parts of the retina depend on contour interaction and attention to the task (Leat, Li, and Epp 1998).

Relationship to Crowding

Crowding refers to the deleterious effects of recognizing an object in the presence of other nearby objects. This is closely related to contour interaction but is considered to be a distinct phenomenon. Flom suggested that crowding is the combined effects of contour interaction, attention, and eye movements (Flom 1991), although more recent studies seem to use these two terms interchangeably. Another commonly accepted distinction between crowding and contour interaction is that the flankers are often more complicated in the case of crowding and simpler, like bars, in the case of contour interaction. In this study, we measured and quantified the magnitude and extent of the contour interaction using visual acuity optotypes commonly used in the pediatric clinic - Lea symbols with four surrounding bars to induce the deleterious effect. Therefore, we will use the term contour interaction instead of crowding in this chapter.

Lea Symbols

One of the most common methods used to measure visual acuity in pediatric populations is with Lea symbols (Hyvärinen, Näsänen, and Laurinen 1980). The test utilizes four different symbols - ball, apple, square, and house. The chart was originally designed for the measurement of visual acuity for children 3-5 years of age. One of the goals was to create a chart with symbols that would be easy to name, and that the child would be able to respond by naming or pointing (to a matched symbol). Hyvärinen et al. evaluated the test-retest reliability of the Lea symbols in seventeen 20-35 year old adults, and the results of the test were compared to results in the same individuals measured with the Snellen E test chart at 6 meters. The reliability of the Lea symbols was found to be 0.94 as compared to 0.96 for the Snellen E.

Since the original introduction of the Lea symbols in 1980, other researchers have evaluated the use of Lea symbols in measuring visual acuity in children. Becker et al. examined young children with Lea symbols in an attempt to establish normal values and interocular differences of visual acuity in normally sighted children (Becker et al. 2002). 385 children (21-93 months of age) were examined. 90 of those children were also re-examined in a hospital setting comparing Lea symbol visual acuity and Landolt C visual acuity. Lea symbol acuity could be measured in 54% of the children. In children older than 36 and 48 months, the success rate was even higher at 76% and 95% respectively. Interocular difference of Lea symbol acuity was one line or less in 90% of the subjects. Unsurprisingly, cooperation was found to increase with age. Ultimately, Lea symbols were found to be useful when measuring acuity in early childhood.

Another group compared the Lea symbol chart to another preliterate acuity chart, the HOTV in a sample of three to five year old children. Similarly, it was found that ease of testing corresponds with increased age. The Lea symbol test was more efficacious in the younger group of three year old children (Hered, Murphy, and Clancy 1997). The Vision in Preschoolers Study Group (VIP) found that both crowded HOTV and Lea symbols were useful in assessing monocular visual acuity in young children between three and five years of age - the crowded HOTV letters were slightly more difficult than the Lea symbols, with the largest difference between acuity results occurring in three-year-old children (Ciner et al. 2003).

Lea symbols have also been evaluated with and without the presence of crowding bars (Gräf, Becker, and Kaufmann 2000). In individuals with amblyopia, Gräf et al. found that a Lea symbol acuity difference of one line (0.1 logMAR) can be considered normal (with or without the presence of contour bars).

Study

Purpose

Understanding the visual challenges for children with visual impairment can be difficult. With well understood types of visual impairment such as retinal disease, reductions in visual functions can be predictable based on the physical location of damage. Conversely, patients with cerebral visual impairment (CVI, formerly cortical visual impairment) have vision loss resulting from an insult to the brain rather than to ocular structures. Understanding this unique form of vision loss, which often develops in an unpredictable fashion, and can go undiagnosed by an eye care provider, (Dutton, McKillop, and Saidkasimova 2006) can pose significant challenges. CVI continues to be an area of growing interest across multiple disciplines including neurobiology, optometry, ophthalmology, and education. It results from damage to any region posterior to the lateral geniculate bodies. Hypoxic brain injury is the most common etiology of CVI (Afshari, Afshari, and Fulton 2001), and other common etiologies include prematurity, hydrocephalus, structural central nervous system abnormalities, and seizures (Khetpal and Donahue 2007).

To compensate for reduced acuity, object size can be increased such that the size of the object exceeds the resolution limit. However, even when the object size is not a limiting factor, recognizing an object can be difficult if there are other objects in close proximity to the object of interest. This phenomenon is known as crowding and it is considered to be one of the major limiting factors for object recognition (Levi and Carney 2009; Pelli and Tillman 2008). Indeed, it has been shown that crowding affects many tasks of daily activities, including acuity (Flom, Weymouth, and Kahneman 1963), reading (Chung, Mansfield, and Legge 1998), face recognition (Whitney and Levi 2011b), reaching and grasping of objects (Bulakowski 2009), all of which have been reported to be difficult tasks for children with CVI (Zihl and Dutton 2015). Parents of children with CVI often report that their child has

difficulty locating objects when there is more than one object present, which is consistent with the crowding effect. Children with CVI experience crowding that is up to three times greater than that experienced by adults (Huurneman et al. 2012). We expect children with CVI will have a greater reduction in visual acuity in the presence of contour interaction, based on information gathered from anecdotal reports as well as two studies (Jacobson et al. 1996; Pike, Holmstrom, and Vries 1994).

Public Health Impact

As discussed in the background chapter, CVI is the leading cause of bilateral visual impairment in children in western countries (Good et al. 2001). According to the American Foundation for the Blind, 30-40% of cases of visual impairment in children are caused by CVI (Roman et al. 2008). Low birthweight and very low birthweight (9.4% of births) are risk factors for developing CVI, in addition to being born preterm (11.4% of births) (Martin et al. 2015). Children born preterm or with low birth weight have a higher risk for visual impairment, including CVI (Vohr et al. 2000). Many babies and families can benefit from a better clinical understanding of CVI.

Methods

Sixty children with cerebral visual impairment (CVI) were retrospectively selected from the Special Visual Assessment Clinic (SVAC) population. The group was composed of 34 males and 26 females ages 3-23 years with a mean age of 9.13 years. The etiologies of visual impairment and disabilities for the subject population are listed in Table 2.1.

Each subject received a comprehensive vision examination that included determination of: refractive error with retinoscopy, eye alignment, vision function (visual acuity, contrast sensitivity, color vision), confrontation visual fields, and ocular health status. Threshold visual acuity was measured using a two-alternative forced choice task in a descending method of limits. The test targets were single apple and house Lea optotypes that each had four flanking bars (commercially available, GoodLite) printed on 5 inch by 5 inch cards. The edge-to-edge (between optotype and bar) spacings were 50% and 100% times the optotype width (determined by manufacturer, see Figure 2.1). The optotypes and flankers were both at 100% contrast. The subjects were tested with both eyes open and with best spectacle correction in place. Pre-testing included training by presentation of suprathreshold symbols at 50 centimeters to establish understanding of the task with the subject pointing at, looking at, or naming either the house or apple symbol. Testing was initiated with the 20/200 (logMAR = 1) equivalent cards at 50 cm using the acuity card procedure (Teller et al. 1986). When the subject responded quickly and accurately, only one or two presentations was given before presenting the next size. Near threshold, more presentations were given and

Etiology	Number of Subjects
Hydrocephalus	5
Microcephaly	7
Periventricular leukomalacia (white matter damage)	9
Joubert Syndrome	2
Hypoxic Ischemic Encephalopathy/cerebrovascular accident/birth trauma	10
Confirmed diagnosis of CVI, unspecified	11
Schizencephaly	1
Cerebellar hypoplasia	1
Infection/drug exposure in utero	2
Injury/malformation of corpus callosum	3
Hemispherectomy	1
Unclear etiology, risk of CVI based on history	8

Table 2.1: Etiologies of CVI subject pool.

the acuity threshold was determined from the symbol size with 3 out of 4 correct responses. Testing distance was increased to 100 or 150 centimeters as needed. The range of acuity targets included 1.5/15 (20/200) to 1.5/1.2 (20/15) with a 150 centimeter viewing distance. Rewards for responding were given as needed (stickers or Cheerios).

Forty-three normally sighted children were also selected from the Pediatric Clinic population. This group was composed of 18 males and 25 females from 3 to 11 years of age with a mean age of 6.09 years. The same vision examination protocol was used, including threshold visual acuity measurements with Lea optotypes with flanking bars at 50% and 100%. The subjects were tested with both eyes open with their best spectacle correction in place. None of the forty-three subjects had any eye disease or vision issues, with the exception of correctable low refractive error.

The study protocol was approved by the Institutional Review Board and followed the tenets of the Declaration of Helsinki.

Results

For children with cerebral visual impairment, an analysis of correlation was performed (Figure 2.2) comparing 50% and 100% logMAR visual acuity for each subject. The visual acuity

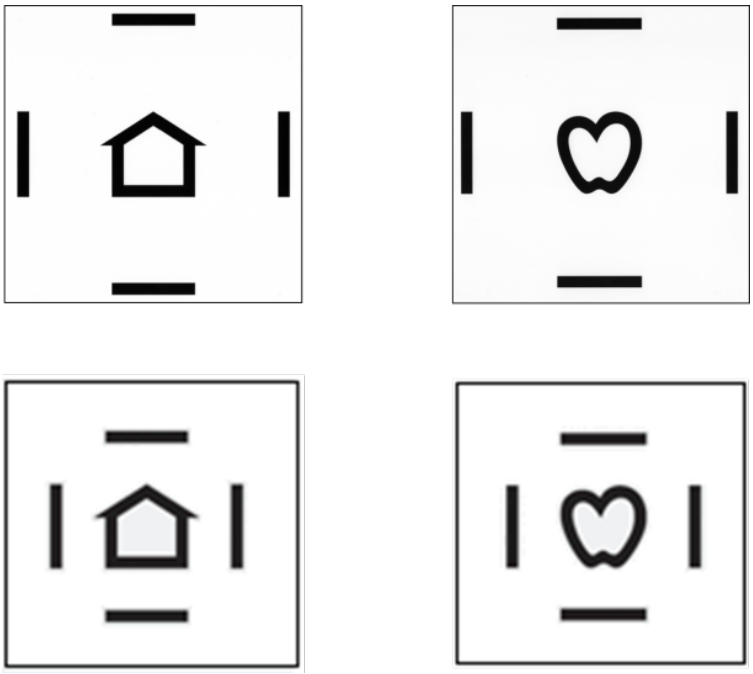

Figure 2.1: Example of 100% and 50% spacing around two Lea optotypes, presented in two alternative forced choice manner.

for eleven subjects fell along the 1:1 line (y = 1.1277x + 0.094, R^2 = 0.896), indicating an identical acuity with both spacings. Only one subject saw slightly better with 50% spacing. All other subjects showed a better visual acuity with 100% spacing as compared to 50% spacing. This was consistent with the expectation that most children with cerebral visual impairment would have a decrease in visual acuity in the presence of increased contour interaction.

A Bland-Altman analysis of the difference in visual acuity measures (100% and 50% spacing) versus their mean (in logMAR) was performed for both groups (Figure 2.3). For the cerebral visual impairment group, mean visual acuity ranged from -0.10 to 1.28 logMAR (20/16 to 20/380). Worse acuity with 50% spacing was found in all but one child, and twelve children showed no difference. For 47 children, the difference ranged from 0.10 to 0.41 logMAR with a trend for an increasing difference between the two acuity measures with worse average acuity. The average difference between the two measures was -0.16 logMAR (equivalent to about a line and a half on a standard acuity chart). On average, the visual acuity for children with CVI was about a line and a half worse with 50% spacing compared to 100% spacing. The slope of the regression equation was found to be significantly different from zero ($p<.0001$), indicating a trend. For the normally sighted group, mean visual acuity ranged from -0.10 to 0.25 logMAR (20/16 to 20/36). Children in the normally sighted group all achieved the same or worse visual acuity with the 50% spacing as compared to the 100% spacing with

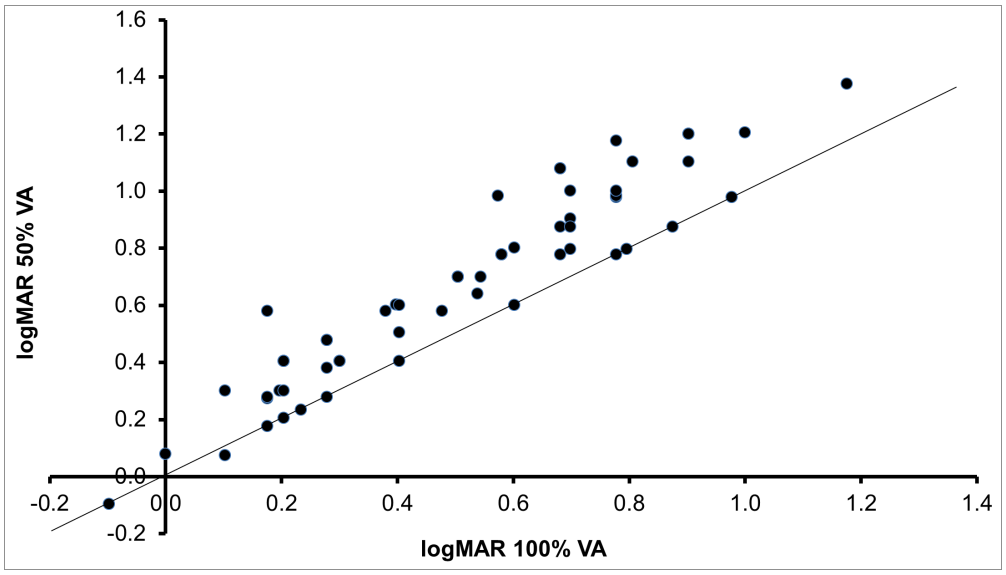

Figure 2.2: Correlation of logMAR VA between both spacings for subjects with CVI. Only one subject falls below the 1:1 line indicating an improved acuity with 50% spacing. All other subjects show equal or worse acuity with 50% spacing.

the exception of one subject who achieved one line worse with 100% spacing. The mean difference was -0.05, about a half of a line worse on average with the 50% spacing compared to the 100% spacing. The mean difference is over three times greater in children with CVI than in normally sighted children.

Discussion

The goal of this study was to quantify the effect of contour interaction due to flanking bars on visual acuity in children with CVI. As expected, the reduction in acuity was greater in the presence of contour bars spaced more closely to the optotype (50% spacing) as compared to greater spacing (100%). This is consistent with previous work done by Manny and Fern that showed a decrease in visual acuity in the presence of contour interaction in preschool children (Fern et al. 1986; Manny, Fern, and Loshin 1987). The expectation is that this effect of contour interaction is greater in children with CVI than in normally sighted children. Manny et al. found that there was a significant decrease in performance when the flanking bars were positioned 0.71 to 1.42 times the angular subtense of the gap for both pre-school children and adults. This is approximately 14% and 28% spacing - that is, their study shows that the distance over which an effect is exhibited in normally sighted children and adults is much closer to the optotype than in the population with CVI measured in our study. This is consistent with our comparison to normally sighted subjects. This difference holds true with these two subject populations: normally sighted children were affected by

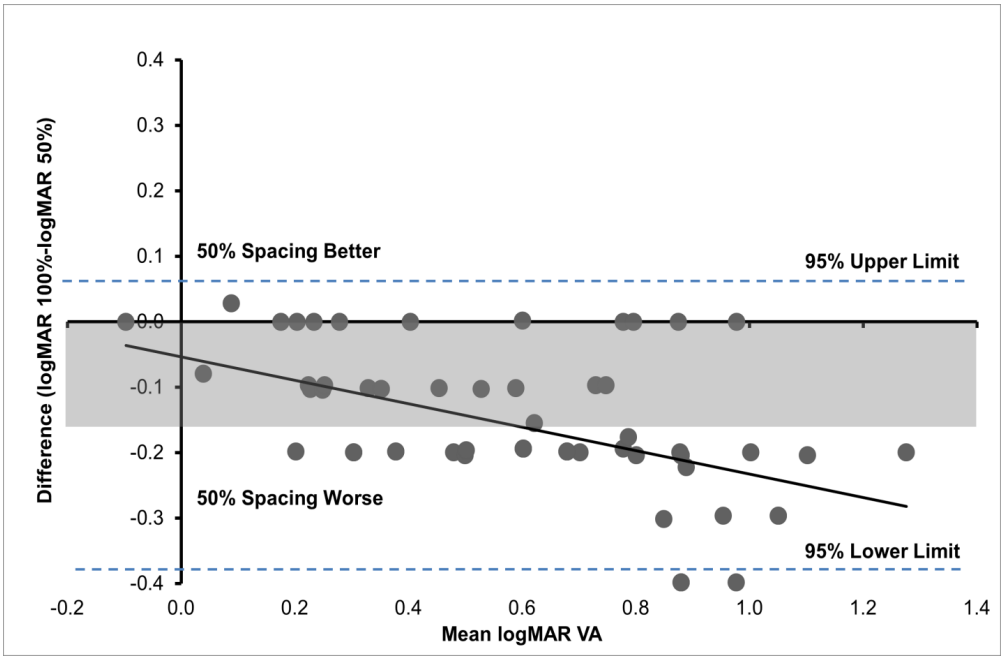

Figure 2.3: Bland-Altman analysis showing the difference in visual acuity measures versus their mean in logMAR in children with CVI.

contour interaction from 50% spacing compared to 100% spacing by an average of half of a line. However, the CVI subject population was affected by contour interaction at 50% spacing an average of one and a half lines. Additionally, Manny et al. determined that the poorer acuity found with charts was not due to contour interaction since the spacing between optotypes is larger than the spacing over which a contour interaction effect is exhibited in normally sighted adults and children.

In another study, 13 preterm children with periventricular leukomalacia (PVL) were examined (Jacobson et al. 1996). Their visual acuity was tested with single optotypes in all 13 children and with linear optotypes in 10 participants (those who were able to complete the task). They concluded that visual impairment due to PVL is characterized by crowding, visual field defects, oculomotor problems, and visual perceptual disturbances. Additionally, they found that color vision and contrast sensitivity are relatively well preserved. They reported crowding ratios in seven participants with acuities in the range of 20/60 to 20/100 with linear optotypes and found a difference of 0.2-0.3 logMAR in linear vs. single (2-3 lines). Our subject population is generally unable to perform linear visual acuity tasks however, these findings are in line with the results of our study which show an average difference of 1.5 lines when comparing visual acuity with 100% and 50% spacing. The expectation is that the crowding bars exhibit some level of contour interaction on the target causing a consistent reduction in visual acuity.

Pike et al. measured crowding ratios in 42 children with one or more of the following lesions documented (severe leukomalacia, large intraventricular hemorrhage, or cerebral infarction) (Pike, Holmstrom, and Vries 1994). They measured the crowding ratio by dividing the visual acuity for linear optotypes by the visual acuity for single optotypes. The linear optotypes used were on the Sonksen-Silver Acuity System (SSAS) and the single optotypes used were the Sheridan-Gardner seven letter test. The criteria were set for abnormally high crowding ratio as greater than or equal to two. Thirteen of the twenty-nine children tested had this amount of crowding (most with acuity around 20/40). Furthermore, abnormal crowding ratios were found to be more common in ischemic than hemorrhagic lesions. Although the visual acuity in this group was better than the average acuity of our population, this continues to be in line with the findings of our study.

Perhaps one of the most extensively studied models of crowding and contour interaction is in individuals with amblyopia. It is well established in the literature that crowding and contour interaction occur in the central visual field of individuals with amblyopia, and this was first reported by Irvine in 1948 (Irvine 1948). More recent work indicates that there is a difference in the effect of crowding in patients with strabismic amblyopia as compared to anisometropic amblyopia (Song, Levi, and Pelli 2014). One important concept in crowding research with respect to amblyopia is the fact that crowding occurs under dichoptic conditions - this means that when a target or flanker is presented to the same or different eyes, the effect of crowding is still observed. This suggests that crowding occurs at a cortical locus (Flom, Heath, and Takahashi 1963). The fact that it occurs in the cortex implies that individuals with cerebral visual impairment may have an analogous visual performance in the presence of crowding as individuals with amblyopia.

Additionally, in the case of subjects with CVI with worse acuity, the effect of the contour interaction was greater as well. This is also somewhat expected as it indicates that in cases of more severe disease which would cause acuity to be worse in general, the effect of contour interaction has a greater effect. Because the loss of acuity is due to damage in the brain, this finding is also intuitive. An additional point of comparison that would be helpful would be to identify how these findings compare to symbols presented in isolation (infinite spacing). Data collection regarding symbols in isolation will be discussed in the following chapter.

These findings may be helpful when making recommendations to teachers and parents. Based on this information, it may be most beneficial to suggest one print size for sight words and a larger print size for words within a paragraph. This could further influence the kerning or tracking of letters, that is, the spacing between letters and words used to maximize readability. Kerning refers to the spacing between two characters to correct for visually uneven spacing (e.g. "cl" may be confused for a "d" without the clarification provided by kerning). On the other hand, tracking applies to the spacing within an entire word. In a study by McLeish, increasing letter spacing in low vision readers improved reading speed and reduced the critical print size for the majority of those tested (McLeish 2007). Our data suggests that

the adjustment made to print size will be dependent on the level of visual acuity reduction in the presence of contour interaction. That is, if an individual has a visual acuity of 20/70, the recommendation may be to increase the print size by 1.5 lines above threshold; for an individual with a visual acuity of 20/200, it would be better to increase the print size by 2 to 2.5 lines above threshold. Finally, because our study utilized flanker bars rather than letters, one would expect that flanking letters (as found in normal text) would pose an even greater challenge for children with cerebral visual impairment.

Conclusions

This study shows a negative effect of contour interaction on visual acuity in children with CVI as well as normally sighted children. This difference is more significant for children with CVI. Educational materials for children with CVI should take into account the reduction in visibility of central letters or symbols when flanking bars or letters are present. The greater the reduction in visual acuity, the greater the reduction in visual acuity with increased crowding. For children with CVI, increasing the size of letters may need to be accompanied by an increase in spacing between letters.

References

1. Afshari, MA, NA Afshari, and AB Fulton. 2001. Cortical Visual Impairment in Infants and Children. International Ophthalmology Clinics 41 (1): 159-69.

2. Andriessen, J.J., and H. Bouma. 1976. Eccentric Vision: Adverse Interactions between Line Segments. Vision Research 16 (1): 71-78.

3. Atkinson, Janette, Oliver Braddick, and Fleur Braddick. 1974. Acuity and Contrast Sensitivity of Infant Vision. Nature 247 (5440): 403-4.

4. Bane, M C, and E E Birch. 1992. VEP Acuity, FPL Acuity, and Visual Behavior of Visually Impaired Children. Journal of Pediatric Ophthalmology and Strabismus 29 (4): 202-9.

5. Banks, M S. 1980. Infant Refraction and Accommodation. International Ophthalmology Clinics 20 (1): 205-32.

6. Banks, M S, and P J Bennett. 1988. Optical and Photoreceptor Immaturities Limit the Spatial and Chromatic Vision of Human Neonates. Journal of the Optical Society of America. A, Optics and Image Science 5 (12): 2059-79.

7. Bansback, N., C. Czoski-Murray, J. Carlton, G. Lewis, L. Hughes, M. Espallargues, C. Brand, and J. Brazier. 2007. Determinants of Health Related Quality of Life and Health State Utility in Patients with Age Related Macular Degeneration: The

Association of Contrast Sensitivity and Visual Acuity. Quality of Life Research 16 (3): 533-43.

8. Becker, R, S Hübsch, M H Gräf, and H Kaufmann. 2002. Examination of Young Children with Lea Symbols. The British Journal of Ophthalmology 86 (5): 513-16.

9. Bouma, H. 1970. Interaction Effects in Parafoveal Letter Recognition. Nature 226: 177-78.

10. Braddick, Oliver, Janette Atkinson, Jennifer French, and Howard C. Howland. 1979. A Photorefractive Study of Infant Accommodation. Vision Research 19 (12): 1319-30.

11. Bulakowski, Paul. 2009. Visuomotor Crowding: The Resolution of Grasping in Cluttered Scenes. Frontiers in Behavioral Neuroscience 3 (November): 1-7.

12. Chung, Susana T.L., J.Stephen Mansfield, and Gordon E. Legge. 1998. Psychophysics of Reading. XVIII. The Effect of Print Size on Reading Speed in Normal Peripheral Vision. Vision Research 38 (19): 2949-62.

13. Ciner, Elise, Lynn Cyert, Velma Dobson, Marjean Taylor Kulp, Maureen Maguire, Bruce Moore, Deborah Orel-Bixler, et al. 2003. Threshold Visual Acuity Testing of Preschool Children Using the Crowded HOTV and Lea Symbols Acuity Tests. Journal of AAPOS 7 (6). Mosby: 396-99.

14. Coates, Daniel Robert, Jeremy M Chin, and Susana T.L. Chung. 2013. Factors Affecting Crowded Acuity: Eccentricity and Contrast. Optometry & Vision Science 90 (7): 996-1005.

15. Dobson, Velma, Graham E. Quinn, R. Michael Siatkowski, John D. Baker, Robert J. Hardy, James D. Reynolds, Michael T. Trese, and Betty Tung. 1999. Agreement between Grating Acuity at Age 1 Year and Snellen Acuity at Age 5.5 Years in the Preterm Child. Investigative Ophthalmology and Visual Science 40 (2): 496-503.

16. Dubowitz, David. 1980. Portable Version of Fantz Box for Assessment of Visual Function. Lancet (London, England) 2 (8207): 1279-80.

17. Dubowitz, Lilly, V Dubowitz Ana Morante, and M Verghote. 1980. Visual Function in the Preterm and Fullterm Newborn Infant.

18. Duncan, J, and G W Humphreys. 1989. Visual-Search and Stimulus Similarity. Psychological Review 96 (3): 433-58.

19. Duncan, R. O., and G. M. Boynton. 2010. Cortical Magnification Factor in Human Primary Visual Cortex Correlates with Vernier Acuity Thresholds. Journal of Vision 2 (7): 129-129.

20. Dutton, G N, E C A McKillop, and S Saidkasimova. 2006. Visual Problems as a Result of Brain Damage in Children. The British Journal of Ophthalmology 90 (8): 932-33.

21. Egeth, Howard. 1977. Attention and Preattention. Psychology of Learning and Motivation 11 (January). Academic Press: 277-320.

22. Ehrt, Oliver, and Robert F Hess. 2005. Foveal Contour Interaction: Detection and Discrimination. Journal of the Optical Society of America. A, Optics, Image Science, and Vision 22 (2): 209-16.

23. Estes, W. K. 1972. Interactions of Signal and Background Variables in Visual Processing. Perception & Psychophysics 12 (3): 278-86.

24. Estes, W K. 1982. Similarity-Related Channel Interactions in Visual Processing. Journal of Experimental Psychology. Human Perception and Performance 8 (3): 353-82.

25. Fantz, Robert L. 1965. Visual Perception From Birth As Shown By Pattern Selectivity. Annals of the New York Academy of Sciences 118 (21): 793-814.

26. Fazzi, Elisa, Sabrina Giovanna Signorini, Stefania Maria Bova, Roberta La Piana, Paola Ondei, Chiara Bertone, Walter Misefari, and Paolo Emilio Bianchi. 2007. Spectrum of Visual Disorders in Children with Cerebral Visual Impairment. Journal of Child Neurology 22 (3): 294-301.

27. Fern, Karen D., Ruth E. Manny, James R. Davis, and Roy R. Gibson. 1986. Contour Interaction in the Preschool Child. American Journal of Optometry & Physiological Optics 63 (5): 313-18.

28. Flom, M.C., G.G. Heath, and E. Takahashi. 1963. Contour Interaction and Visual Resolution: Contralateral Effects. Science 142 (3594): 979-80.

29. Flom, Mert. 1991. Contour Interaction and the Crowding Effect. Problems in Optometry 3 (2): 237-57.

30. Flom, Mert, Frank W Weymouth, and Daniel Kahneman. 1963. Visual Resolution and Contour Interaction. Journal of the Optical Society of America 53 (9): 1026-32.

31. Good, W. V., C. Hou, and A. Norcia. 2012. Spatial Contrast Sensitivity Vision Loss In Children With Cortical Visual Impairment. Investigative Ophthalmology & Visual Science 53 (12): 7730-34.

32. Good, William V. 2001. Development of a Quantitative Method to Measure Vision in Children with Chronic Cortical Visual Impairment. Trans Am Ophthalmol Soc 99 (2): 253-69. Good, William V., James E. Jan, Susan K. Burden, A. Skoczenski, and T Rowan Candy. 2001. Recent Advances in Cortical Visual Impairment. Developmental Medicine and Child Neurology 43: 56-60.

33. Gräf, M H, R Becker, and H Kaufmann. 2000. Lea Symbols: Visual Acuity Assessment and Detection of Amblyopia. Graefes Archive for Clinical and Experimental Ophthalmology = Albrecht von Graefes Archiv Fr Klinische Und Experimentelle Ophthalmologie 238 (1): 53-58.

34. Gwiazda, Jane, Sarah Brill, Indra Mohindra, and Richard Held. 1978. Infant Visual Acuity and Its Meridional Variation. Vision Research 18 (11): 1557-64.

35. Hainline, Louise, Patricia Riddell, Jillian Grose-Fifer, and Israel Abramov. 1992. Development of Accommodation and Convergence in Infancy. Behavioural Brain Research 49 (1): 33-50.

36. Hered, Robert W., Suzanne Murphy, and Mary Clancy. 1997. Comparison of the HOTV and Lea Symbols Charts for Preschool Vision Screening. Journal of Pediatric Ophthalmology and Strabismus 34 (1): 24-28.

37. Howland, H C, J Atkinson, O Braddick, and J French. 1978. Infant Astigmatism Measured by Photorefraction. Science (New York, N.Y.).

38. Huurneman, Bianca, F Nienke Boonstra, Ralf Fa Cox, Antonius Hc Cillessen, and Ger Van Rens. 2012. A Systematic Review on Foveal Crowding in Visually Impaired Children and Perceptual Learning as a Method to Reduce Crowding. BMC Ophthalmology 12 (1). 27.

39. Hyvärinen, L, R Näsänen, and P Laurinen. 1980. New Visual Acuity Test for Pre-School Children. Acta Ophthalmologica 58 (4): 507-11.

40. Irvine, SR. 1948. Amblyopia Ex Anopsia. Observations on Retinal Inhibition, Scotoma, Projection, Light Difference Discrimination and Visual Acuity. Transactions of the American Ophthalmological Society 46: 527-75.

41. Jacobson, L, U Ek, E Fernell, O Flodmark, and U Broberger. 1996. Visual Impairment in Preterm Children with Periventricular Leukomalacia–Visual, Cognitive and Neuropaediatric Characteristics Related to Cerebral Imaging. Developmental Medicine and Child Neurology 38: 724-35.

42. Khetpal, Vijay, and Sean P. Donahue. 2007. Cortical Visual Impairment: Etiology, Associated Findings, and Prognosis in a Tertiary Care Setting. Journal of American Association for Pediatric Ophthalmology and Strabismus 11 (3): 235-39.

43. Kooi, Frank L., Alexander Toet, Srimant P. Tripathy, and Dennis M. Levi. 1994. The Effect of Similarity and Duration on Spatial Interaction in Peripheral Vision. Spatial Vision 8 (2): 255-79.

44. Kothe, Angela C., and David Regan. 1990. Crowding Depends on Contrast. Optometry & Vision Science 67 (4): 28386.

45. Kröse, BJA. 1987. Biological Cybernetics. Biological Cybernetics 55: 289-98.

46. Leat, Susan J, Wei Li, and Karen Epp. 1998. Crowding in Central and Eccentric Vision: The Effects of Contour Interaction and Attention, 504-12.

47. Levi, Dennis M, and Thom Carney. 2009. Crowding in Peripheral Vision: Why Bigger Is Better. Current Biology: CB 19 (23): 1988-93.

48. Levi, Dennis M, Srividhya Hariharan, and Stanley A Klein. 2002. Suppressive and Facilitatory Spatial Interactions in Peripheral Vision: Peripheral Crowding Is Neither Size Invariant nor Simple Contrast Masking. Journal of Vision 2 (2): 3.

49. Lim, Mira, Janet S Soul, Ronald M Hansen, Luisa Mayer, Anne Moskowitz, and Anne B Fulton. 2005. Development of Visual Acuity in Children with Cerebral Visual Impairment. Archives of Ophthalmology 123 (9): 1215-20.

50. Manny, Ruth E., Karen D. Fern, and David S. Loshin. 1987. Contour Interaction Function in the Preschool Child. American Journal of Optometry Physiological Optics 64 (9): 686-92.

51. Marron, J A, and I L Bailey. 1982. Visual Factors and Orientation-Mobility Performance. American Journal of Optometry and Physiological Optics 59 (5): 413-26. Martin, Joyce A, Brady E Hamilton, D Ph, Michelle J K Osterman, Sally C Curtin, and T J Mathews. 2015. National Vital Statistics Reports. Vol. 64.

52. McLeish, Eve. 2007. A Study of the Effect of Letter Spacing on the Reading Speed of Young Readers with Low Vision. The British Journal of Visual Impairment 25 (2): 133-43.

53. Mohindra, I. 1977. A Non-Cycloplegic Refraction Technique for Infants and Young Children. Journal of the American Optometric Association 48 (4): 518-23.

54. Morante, A, L M Dubowitz, M Leven, and V Dubowitz. 1982. The Development of Visual Function in Normal and Neurologically Abnormal Preterm and Fullterm Infants. Developmental Medicine and Child Neurology 24 (6): 771-84.

55. Nazir, Tatjana A. 1992. Effects of Lateral Masking and Spatial Precueing on Gap-Resolution in Central and Peripheral Vision. Vision Research 32 (4): 771-77.

56. Owsley, C, and M E Sloane. 1987. Contrast Sensitivity, Acuity, and the Perception of Real-World Targets. British Journal of Ophthalmology 71 (10): 791-96.

57. Pelli, D. G., Melanie Palomares, and Najib J. Majaj. 2004. Crowding Is Unlike Ordinary Masking: Distinguishing Feature Integration from Detection. Journal of Vision 4 (12): 12.

58. Pelli, Denis G, and Katharine A Tillman. 2008. The Uncrowded Window of Object Recognition. Nature Neuroscience 11 (10): 1129-35.

59. Pelli, Denis G, Katharine A Tillman, J Freeman, Michael Su, Tracey D Berger, and Najib J Majaj. 2007. Crowding and Eccentricity Determine Reading Rate. Journal of Vision 7 (2): 20.

60. Pike, MG, G Holmstrom, and LS De Vries. 1994. Patterns of Visual Impairment Associated with Lesions of the Preterm Infant Brain. Developmental Medicine and Child Neurology 36: 849-62.

61. Polat, Uri, and Dov Sagi. 1993. Lateral Interactions between Spatial Channels: Suppression and Facilitation Revealed by Lateral Masking Experiments. Vision Research 33 (7): 993-99.

62. Roman, C., L. Baker-Nobles, G. Dutton, T. Luiselli, B. Flener, J. Jan, A. Lantzy, et al. 2008. Statement on Cortical Visual Impairment. American Foundation for the Blind. 2008.

63. Shiffrin, R M, and G T Gardner. 1972. Visual Processing Capacity and Attentional Control. Journal of Experimental Psychology 93 (1): 7282.

64. Song, Shuang, DM Levi, and DG Pelli. 2014. A Double Dissociation of the Acuity and Crowding Limits to Letter Identification, and the Promise of Improved Visual Screening. Journal of Vision 14: 1-37.

65. Teller, Davida, Mary Alice McDonald, Karen Preston, S. Lawson Sebris, and Velma Dobson. 1986. Assessment of Visual Acuity in Infants and Children: The Acuity Card Procedure. Developmental Medicine & Child Neurology 28 (6): 779-89.

66. Teller, Davida, Ralph Morse, Richard Borton, and David Regal. 1974. Visual Acuity for Vertical and Diagonal Gratings in Human Infants. Vision Research 14 (12). Pergamon: 1433-39.

67. Toet, Alexander, and Dennis M. Levi. 1992. The Two-Dimensional Shape of Spatial Interaction Zones in the Parafovea. Vision Research 32 (7): 1349-57.

68. Treisman, Anne, and Janet Souther. 1985. Journal of Experimental Psychology: General Processing of Separable Features. Search 114 (3): 285-310.

69. Tripathy, Srimant P., and Patrick Cavanagh. 2002. The Extent of Crowding in Peripheral Vision Does Not Scale with Target Size. Vision Research 42 (20): 2357-69.

70. Vohr, B R, L L Wright, a M Dusick, L Mele, J Verter, J J Steichen, N P Simon, et al. 2000. Neurodevelopmental and Functional Outcomes of Extremely Low Birth Weight Infants in the National Institute of Child Health and Human Development Neonatal Research Network, 1993-1994. Pediatrics 105 (6): 1216-26.

71. Watson, Tonya, Deborah Orel-Bixler, and Gunilla Haegerström-Portnoy. 2010. Early Visual Evoked Potential Acuity and Future Behavioral Acuity in Cortical Visual Impairment. Optometry & Vision Science 87 (2): 80-86.

72. Whitney, David, and Dennis M Levi. 2011a. Visual Crowding: A Fundamental Limit on Conscious Perception and Object Recognition. Trends Cogn Sci 15 (4): 160-68.

73. Whitney, David, and Dennis M Levi. 2011b. Visual Crowding: A Fundamental Limit on Conscious Perception and Object Recognition. Trends in Cognitive Sciences 15 (4): 160-68.

74. Wiesel, Torsten N, and David H Hubel. 1963. Responses in Striate Deprived of Vision Cortex of One Eye. Journal of Neurophysiology 26: 1003-17.

75. Wolford, George, and Lawrence Chambers. 1983. Lateral Masking as a Function of Spacing. Perception & Psychophysics 33 (2): 129-38.

76. Yuodelis, Cristine, and A Hendrickson. 1986. A Qualitative and Quantitative Analysis of the Human Fovea during Development. Vision Research 26 (6): 847-55.

77. Zihl, Josef, and Gordon N Dutton. 2015. Cerebral Visual Impairment in Children.

Chapter 3

Critical spacing of contour interaction

Background

Cerebral Visual Impairment - Overview

Cerebral visual impairment (CVI) is the leading cause of vision loss in children in industrialized nations and results from an insult to the developing brain. As described in the preceding chapter, children with CVI have more difficulty with identifying symbols in the presence of contours. The goal of this study was to determine the critical spacing of contour interaction with contour bars in children with CVI as compared to a group of normally sighted children. If critical spacing can be quantified more thoroughly, then better recommendations can be made to the child's care team with respect to optimal spacing for accessing educational and other materials.

Visual Challenges for Children with CVI

Studies and case reports identify complex visual patterns, arrays, and scenes to be visually challenging for children with CVI. In their study, Dutton et al. identified various behaviors underlying dorsal stream dysfunction that can contribute to an impaired ability to handle complex visual scenes and tasks such as finding a toy in a toy box, finding an item of clothing in a pile of clothing, or seeing a distant object even if it exceeds their resolution limit. This can also create challenges when identifying people in a group, crowded places, and of course, difficulties with reading printed materials (Dutton, McKillop, and Saidkasimova 2006).

Jan et al. evaluated common behaviors of children with CVI. The children varied in age from 6 months to 17 years, with a mean age of 5.5 years. In addition to some variability in visual acuity and visual function, the subjects also showed a preference for using touch to identify objects, variability in visual field defects, and looking away while reaching (Jan et al. 1987). This tendency to look away while reaching was also described by (Good et al. 2001); other behaviors include paying greater attention to moving objects than stationary

ones (Jan et al. 1987) and light gazing (Jan, Groenveld, and Sykanda 1990) or photophobia (Jan, Groenveld, and Anderson 1993).

In their recent review on the CVI literature, Philip and Dutton identified characteristics of visual dysfunction in children with CVI. They reported that patterns of visual dysfunction can be quite varied in CVI. Total blindness is rare. In higher-functioning children, functional visual acuity usually tends to be greater than twice the level of visual acuity when tested with Lea symbols or crowded and uncrowded visual acuity charts with pictures and letters. Generally speaking, children with CVI have normal color vision. Visual field deficit is related to the location of the specific visual pathway damage. Furthermore, contrast sensitivity can be reduced but is not always (Philip and Dutton 2014).

Critical Spacing Curves

As discussed in Chapter 2, crowding refers to the deleterious effects of recognizing an object in the presence of other nearby objects. This is closely related to contour interaction, but is considered to be a distinct phenomenon. Flom suggested that crowding is the combined effects of contour interaction, attention, and eye movements (Flom 1991), although more recent studies seem to use these two terms interchangeably. There are two major models utilized to discuss contour interaction or feature interaction. One model describes how two nearby items compete for a limited set of feature detectors (Estes 1972). These feature detectors transform the incoming information and make comparisons. The second model posits that features of a character drift over time. This work demonstrated that several processes contribute to crowding including response competition, distribution of attention, perceptual grouping, and contour interaction.

Crowding has been extensively studied for decades and is an established element in understanding visual perception. Although crowding is a distinct phenomenon that differs from contour interaction, inferences can be drawn from studies that have focused on crowding as it is typically a more complex phenomenon of which contour interaction is a primary component.

Bouma found that for complete visual isolation to occur at a given eccentricity ϕ degrees, no other letters should be present within 0.5ϕ degrees (Bouma 1970). The general goal of crowding experiments is to quantify the critical spacing and to compare it under different conditions. The critical spacing is the distance at which flanks degrade performance.

Bouma's law regarding the critical spacing of crowding has been well studied in the literature. Many studies have demonstrated that the level of crowding is proportional to the distance from fixation and is dependent on position and direction in the visual field. This directly relates to the visual cortex. That is, the cortical magnification factor is dependent on eccentricity and can be mapped reliably to primary visual cortex (V1) (Pelli and Tillman

2008). Although these studies were primarily focused on normally sighted individuals or individuals with amblyopia, it demonstrates the important relationship that exists between critical spacing and visual cortex. Therefore, one could posit that an individual with cortical damage (or other brain damage) may have a disruption of this relationship and therefore critical spacing.

There are three general approaches to quantify crowding. The first utilizes a fixed target size which is identified some percentage of the time in isolation (e.g. 90%) and then flankers are introduced at various distances. This allows for quantification of both strength and extent of crowding. The second approach is to measure a threshold for identifying the target and then vary the target and flank parameters such as size, distance, etc. The final approach involves measuring flanked and unflanked acuity. Comparing to the unflanked acuity controls for the confounding of size and spacing in the measurement. It is important to note the threshold criterion in a given study on crowding, as well as if the experimenter is using center to center or edge to edge separation in their measurements (Levi 2008). Failure to understand the method of analysis used may skew interpretation of presented results.

One concept proposed by Pelli is that the external world is mapped onto V1 retinotopically. As a result of this mapping to the primary visual cortex, for an object to be recognized, it must be separated in the visual cortex by at least six millimeters radially and at least one millimeter circumferentially. This means that unless objects are sufficiently separated beyond a given critical spacing, the objects will be perceived as a jumble rather than distinct objects. The similarity of flankers to the target affects the amount (or amplitude) but not the spatial extent of the crowding. There are three main supporting components to this finding: the necessary critical spacing in the visual field is proportional to the eccentricity of the objects; the critical spacing is independent of object size and kind; the position in V1 on the cortical surface is the log of the eccentricity in the visual field (Pelli 2008).

It has been well established for decades that identification of flanked letters improves with letter separation (Bouma 1970). Furthermore, critical spacing has been studied in various populations to determine the extent to which two elements may affect the legibility of the other (e.g. flanking bars surrounding an optotype). It is common to analyze the effects of critical spacing on crowding and contour interaction. One of the more frequently evaluated populations for crowding is individuals with amblyopia. Crowding as modeled by critical spacing accounts for the limits seen on reading in amblyopic patients (Levi, Song, and Pelli 2007). Interestingly, Levi et al. also found that in normally sighted subjects and in amblyopic subjects, the critical spacing for crowding and reading was equal. That is, for individuals with amblyopia, crowding poses limitations on reading by determining the size of the uncrowded span or the number of characters which may be presented without causing crowding. The crowded span determines reading rate independent of the spacing of letters within the span.

Critical Spacing in Amblyopia

There are a number of approaches to quantifying critical spacing in a given study. One approach is to fit a cumulative Gaussian function and estimate the target to flank distance for a set level of performance (e.g. 75% correct) (Toet and Levi 1992). Another approach is to fit a curve to the threshold versus flank distance to quantify the magnitude and degree. As mentioned before, it is important to note if an investigator used center to center separation of target and flankers or edge to edge spacing when interpreting the results of a study. This difference in reporting creates a discrepancy in which some investigators report critical spacing to be about 0.1 times the target eccentricity (edge to edge) such as in (Levi, Hariharan, and Klein 2002) and other studies report that critical spacing is 0.5 times the target eccentricity (center to center) such as in (Bouma 1970; Toet and Levi 1992), and others.

Crowding and contour interaction have both been extensively studied in people with amblyopia. Amblyopia has served as an excellent model for our understanding of crowding. This phenomenon has been discussed for many years with respect to amblyopia and continues to be an area of continued research interest. Calculating critical spacing relies on making assumptions - one such assumption made in understanding critical spacing of crowding in amblyopia is found in the uncrowded-span model which joins Bouma's eccentricity dependent model of crowding (Bouma 1970) with Legge, Mansfield, and Chung's idea of proportionality of reading rate relative to visual span (Legge, Mansfield, and Chung 2001). In this model, Legge et al. describe this joint model in which spatiotemporal characteristics of the visual span limit reading speed in central vision, and that in the periphery, the fact that the visual span shrinks is the main limiting factor for reading speed. Pelli defined the uncrowded span as the number of character positions in a line of text that are uncrowded (exceeding the critical spacing) (Pelli et al. 2007). Pelli's model focuses on the uncrowded span and demonstrates that this model explains the shape of reading rate curves. Furthermore, their work showed that critical spacing for letter identification was able to predict both critical spacing and span of reading.

From previous studies on crowding in amblyopia, it is known that crowding occurs under dichoptic conditions - this means that when a target or flanker is presented to the same or different eyes, the effect of crowding is still observed. This suggests that crowding occurs at a cortical locus (Flom, Heath, and Takahashi 1963). For this reason, amblyopia may be a reasonable model to look to when studying CVI as individuals with CVI may have analogous performance in the presence of crowding to those with amblyopia.

Expected Critical Spacing in Children

Normally sighted children show more foveal crowding than adults, both in terms of target-flanker similarity and linear presentation (optotypes presented on a crowded line). They

exhibit more contour interaction which does not mature until age nine. Attention and eye movements are likely to mature around age seven, but can have an effect which extends beyond age seven (Norgett and Siderov 2014).

When discussing critical spacing of contour interaction, it is helpful to formulate context for expectations regarding contour interaction in children without visual impairment. In two landmark papers, Manny and Fern and others evaluated contour interaction in preschool aged children. They set out to study whether the reduction in performance of children tested with isolated versus multiple optotypes was due to contour interactions or due to another phenomenon. They measured visual acuity in children aged 2-7 using Landolt C's and O's. Their results showed that preschool children are affected by contour interaction (Fern et al. 1986).

In a later study, they showed a significant decrease in performance when the flanking bars were positioned 0.71 to 1.42 times the angular subtense of the gap for both children and adults. However, they pointed out that acuity charts with multiple letters per line are often spaced more widely. Therefore, another conclusion was that the reduction in acuity measured with linear charts compared to isolated symbol presentation is not necessarily solely due to contour interaction (Manny, Fern, and Loshin 1987).

Critical Spacing in CVI

There are no studies to date that have quantified the magnitude and extent of critical spacing of crowding or contour interaction in children with CVI. However, some studies have looked at crowding ratios as a method of quantifying crowding.

One study evaluated 13 preterm children with periventricular leukomalacia (PVL) (Jacobson et al. 1996). Their visual acuity was tested with single optotypes in all 13 children and with linear optotypes in 10 participants (those who were able to complete the task). They concluded that visual impairment due to PVL is characterized by crowding, visual field defects, oculomotor problems, and visual perceptual disturbances. Furthermore, they found that certain visual functions were well preserved in PVL such as color vision and contrast sensitivity. They reported crowding ratios in seven participants with acuities in the range of 20/60 to 20/100 with linear optotypes and found a difference of 0.2-0.3 logMAR in linear vs. single (2-3 lines) presentations. This does not directly measure critical spacing, however, it is in line with our findings that the critical spacing is greater in children with CVI. To directly measure critical spacing, it would be necessary to vary the distance between target and flanker systematically rather than using a ratio of linear to single symbol presentations.

Another study by Pike et al. measured crowding ratios in 42 children with one or more of the following lesions documented (severe leukomalacia, large intraventricular hemorrhage, or cerebral infarction) (Pike, Holmstrom, and Vries 1994). They measured the crowding

ratio by dividing the visual acuity for linear optotypes (using Sonksen-Silver Acuity System) by the visual acuity for single optotypes (using Sheridan-Gardner seven letter test). The researchers set the criteria for abnormally high crowding ratio as being greater than or equal to two. Thirteen of the twenty-nine children tested had this amount of crowding (most with acuity around 20/40). They also found that abnormal crowding ratios were more common in ischemic than hemorrhagic lesions. Once again, this is in line with the findings of this study, and one would anticipate that if critical spacing had been measured in this study, that it would show a similar trend to our data.

Applicability of Contour Interaction

Although contour interaction is a basic component of crowding and is not the same thing as crowding, it can still be a useful parameter when characterizing visual difficulties in children with CVI. If contour interaction is affected significantly in CVI, we can assume that crowding would also be affected. Of course, further investigations aimed at crowding in particular still remain to be done and this will be the only way to obtain definitive data regarding crowding as a distinct phenomenon. In the meantime, a reduction in contour interaction would still be expected to affect vision in children with CVI, not only with reading tasks, but also in their day to day life, especially in cluttered, busy, and crowded situations.

Study

Purpose

As discussed in more detail in Chapter 2, the first preliminary study showed that there is a reduction in acuity with contour bars that are spaced 50% versus 100% of the optotype size away from the optotype of interest in children with CVI. The goal of that study was to quantify the effect of contour interaction due to flanking bars on acuity in children with CVI. As expected, the reduction in acuity was greater in the presence of contour bars spaced more closely (50% spacing) as compared to greater spacing (100% spacing). This is consistent with previous work done by Manny and Fern who showed a decrease in acuity in the presence of contour interaction in preschool children (Fern et al. 1986), (Manny, Fern, and Loshin 1987). The expectation is that this effect of contour interaction is greater in children with CVI than in normally sighted children.

To have a better understanding of the critical spacing of contour interaction, isolated symbols were also measured in children with CVI. Additionally, normally sighted children were also tested. Having a better understanding of the extent of contour interaction can be useful when determining the differences between clinical measurements in isolation compared to more realistic visual targets with surrounding flankers. Most objects that are presented in real world settings are not presented in isolation. Therefore, it can be helpful to know the

Etiology	Number of Subjects
Hydrocephalus	1
Microcephaly	2
Periventricular leukomalacia (white matter damage)	3
Joubert Syndrome	1
Hypoxic Ischemic Encephalopathy/cerebrovascular accident/birth trauma	2
Confirmed diagnosis of CVI, unspecified	2
Infection/drug exposure in utero	1
Injury/malformation of corpus callosum	1
Hemispherectomy	1
Unclear etiology, risk of CVI based on history	5

Table 3.1: Etiologies of CVI subject pool.

extent to which a child with CVI may be more greatly affected by the effects of contour interaction.

Materials and Methods

Binocular visual acuity was measured during a comprehensive vision examination for 19 children (ages 4-20 years; mean 9.6 years) presenting with a diagnosis of CVI (etiologies listed in Table 3.1) and 37 normally sighted children (ages 3-11 years; mean 6.2 years). An additional group of 43 children (ages 3-23; mean 9.13 years) with CVI with only two of the three measurements (50% and 100% spacing) were also included when fitting a critical spacing template to the data.

Single Lea symbols with contour flanker bars at 50%, 100%, and infinite (unflanked) spacing were presented in a two-alternative forced choice manner using the apple and the house as the test optotypes (see Figure 3.1). Visual acuity thresholds were determined using the modified acuity card procedure by observation of the child's eye gaze, pointing, and/or naming of the optotype. A two line best fit template was used to construct a curve that indicates the critical spacing for each population (at the intersection of the two lines). To determine confidence intervals, Monte Carlo simulations were generated based on the subject data according to methods used by Coates, Chin, and Chung (2013) and Kingdom and Prins (2010).

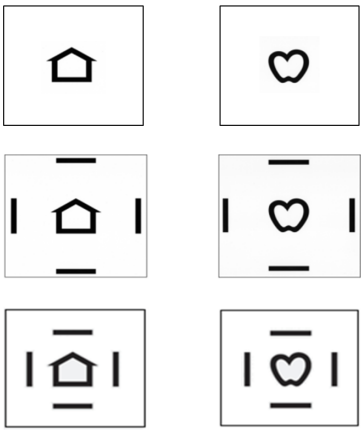

Figure 3.1: Visual acuity targets: Lea symbols with varying flanker spacing (schematic - not necessarily to scale).

Results

For the 19 children with CVI, visual acuity ranged from 0.0 to 1.38 logMAR using 100% Lea symbols (which yielded better acuity). For the same group of 19 children, the mean difference in visual acuity was 0.24 logMAR for isolated vs. 50% spacing, 0.16 logMAR for 100% vs. 50% spacing, and 0.08 logMAR for isolated vs. 100% spacing.

In normally sighted children, the mean difference in visual acuity was 0.05 logMAR for isolated vs. 50% spacing, 0.03 logMAR for 100% vs. 50% spacing, and 0.02 logMAR for isolated vs. 100% spacing. A two-line best fit template was fit to the data for children with CVI and normally sighted children. The critical spacing was found to be 1.11 log units of spacing for the CVI group and 0.47 log units of spacing for the normal group. 44 additional children with CVI were included with two measurements (50% and 100%) and were fit to the template. Figures 3.2 and 3.3 show the distribution of the data and the critical spacing point for both groups. Note that the critical spacing is shifted to the right for the CVI group, and also that the visual acuity measurements are higher in logMAR (corresponding to poorer acuity) for the CVI group as a whole compared to the normally sighted group.

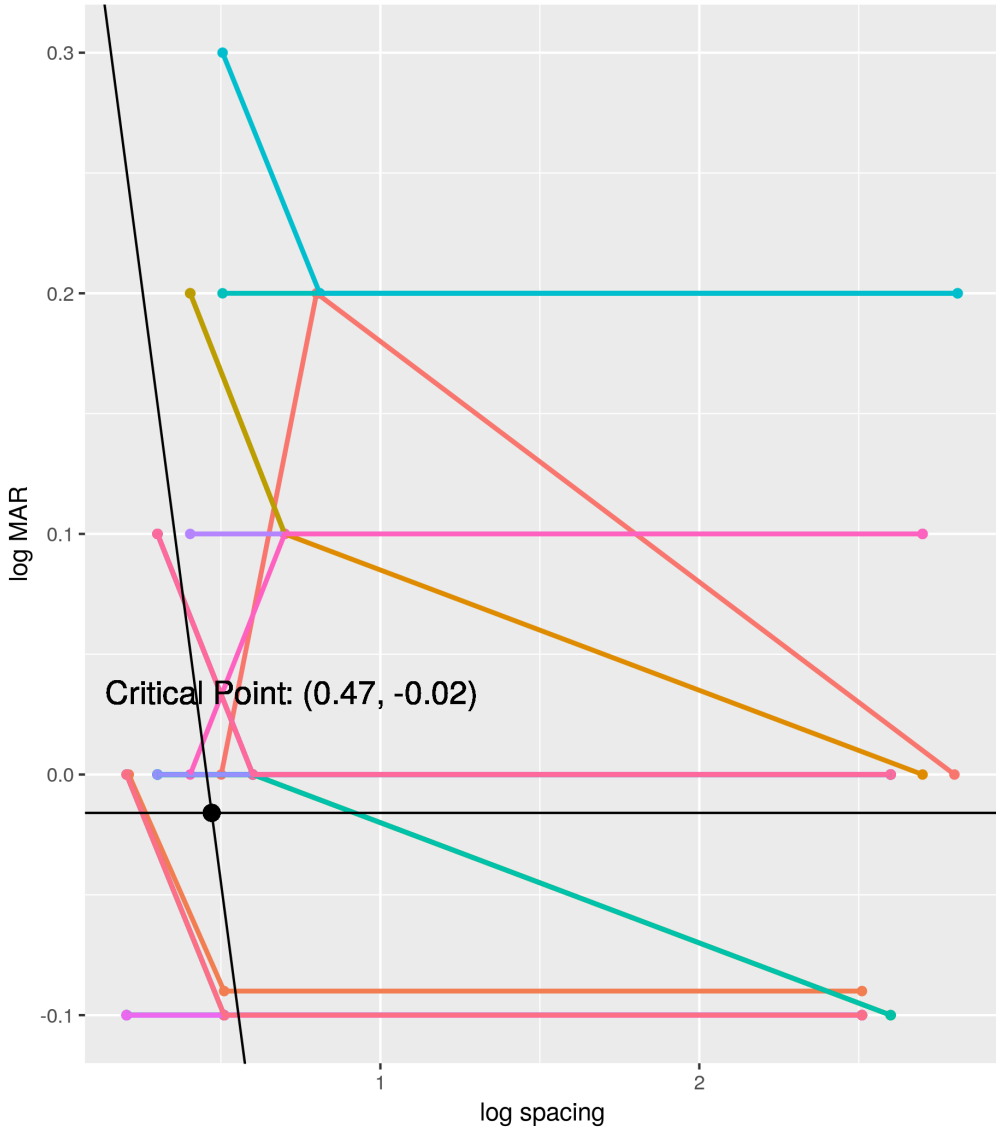

Figure 3.2: Critical spacing curves for normally sighted children. The point of intersection is based on the average across subjects. For normally sighted children, the critical spacing was found to be 0.47 log units of spacing.

logMAR50%	logMAR100%	logMARiso
1.08	0.68	0.58
1.08	0.68	0.58
0.20	0.20	0.00
0.30	0.00	0.00
0.78	0.58	0.48
1.38	1.08	1.07
1.00	0.70	0.70
0.40	0.20	0.10
0.80	0.60	0.60
0.70	0.54	0.40
-0.10	-0.10	-0.10
0.30	0.20	0.00
0.20	0.20	0.30
0.40	0.40	0.40
0.18	0.18	0.18
0.88	0.88	0.78
0.88	0.68	0.58
0.78	0.78	0.48
0.28	0.28	0.28

Table 3.2: Raw visual acuity data for children with CVI. Most children showed an improvement in visual acuity with decreasing contour.

Case Report Comparison

Case Report 1

G.R. is a 4 year old male who presented for a comprehensive vision exam as a new patient to the Special Visual Assessment Clinic (SVAC). G.R. was born at 37.5 weeks and his medical history is significant for seizures, ischemic brain injuries, mini-strokes, cerebral palsy, developmental delay, and cerebral visual impairment. The cause of his CVI is attributed to hypoxic ischemic injury. He is not taking any medications. His refractive error is +1.75DS in both eyes with cycloplegic retinoscopy. He has an intermittent exotropia but his eyes remain well aligned during examination. With the Cardiff Acuity Test he is able to locate but not identify targets at the 20/20 visual acuity level. His logMAR visual acuities for isolated, 100%, and 50% spacing are 0.48 logMAR (20/60), 0.58 logMAR (20/76), and 0.78 logMAR (20/120), respectively. His Cambridge Contrast sensitivity is reduced to 1% (measured in Michelson contrast). His color vision and visual fields are normal. G.R. is a good example of an individual who follows the general pattern expected with increased proximity of contours

logMAR50%	logMAR100%	logMARiso
0.00	0.20	0.00
0.00	-0.09	-0.09
0.20	0.10	0.10
0.20	0.10	0.00
0.00	0.00	0.00
-0.10	-0.10	-0.10
0.20	0.10	0.10
0.00	0.00	-0.10
0.00	0.00	0.00
-0.10	-0.10	-0.10
0.00	-0.10	-0.10
0.10	0.00	0.00
-0.10	-0.10	-0.10
0.00	0.00	-0.10
0.00	-0.10	-0.10
0.00	0.00	0.00
0.10	0.00	0.00
0.00	0.00	-0.10
0.20	0.20	0.20
0.30	0.20	0.20
0.00	0.00	0.00
0.10	0.00	0.00
0.00	0.00	0.00
-0.10	-0.10	-0.10
-0.10	-0.10	-0.10
0.00	-0.10	-0.10
0.00	0.00	0.00
0.10	0.10	0.10
-0.10	-0.10	-0.10
-0.10	-0.10	-0.10
-0.10	-0.10	-0.10
0.00	-0.10	-0.10
0.10	0.00	0.00
0.00	0.10	0.10
0.10	0.00	0.00
0.10	0.00	0.00
0.00	-0.10	-0.10

Table 3.3: Raw visual acuity data for children with normal vision. None of the children show a significant effect between varying levels of contour.

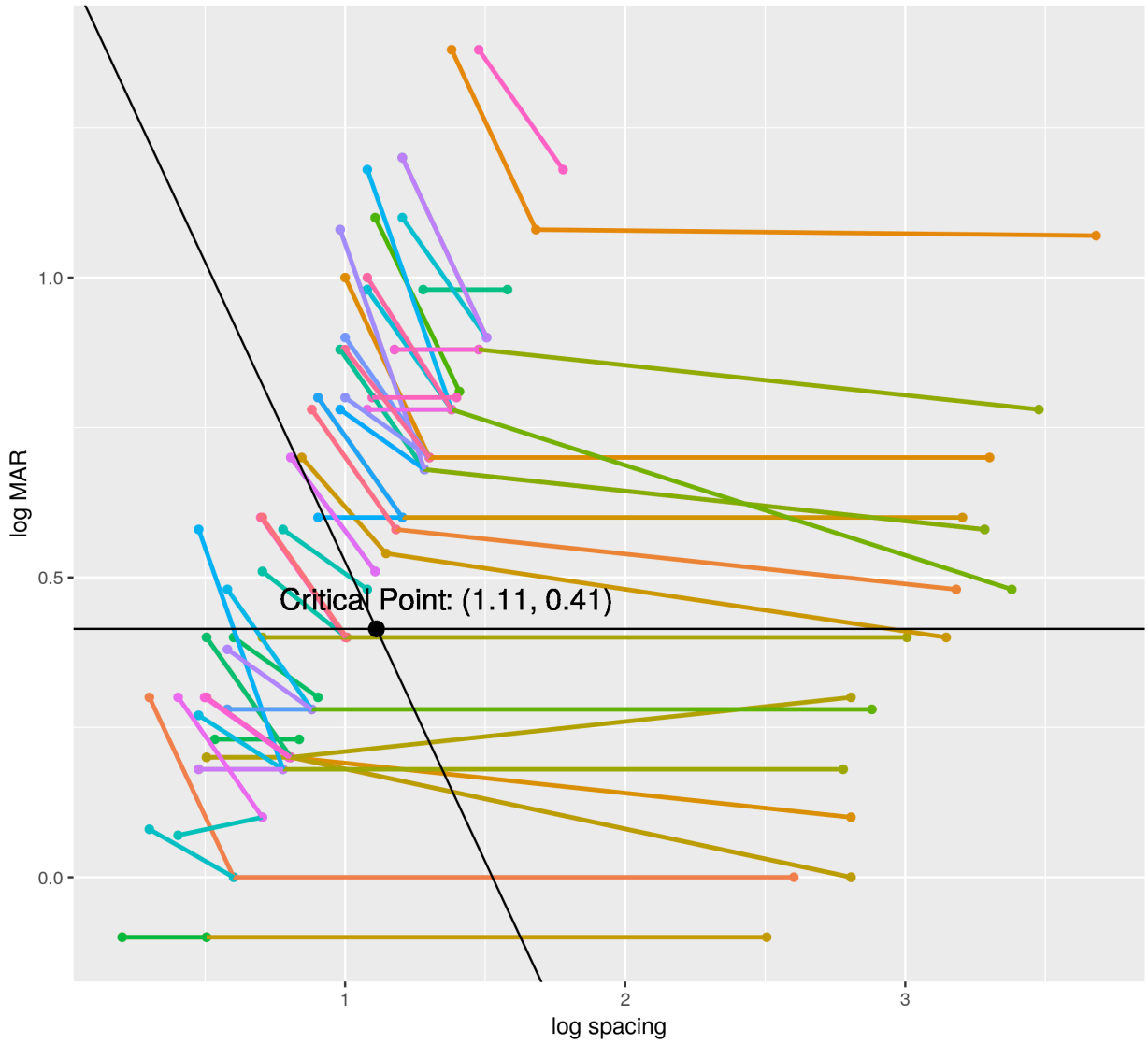

Figure 3.3: Critical spacing curves for children with CVI. The point of intersection is based on the average across subjects. For children with CVI, the critical spacing was found to be 1.11 log units of spacing. This value is of particular interest when compared to the critical spacing found for children with normal vision. That is, children with CVI show a significantly larger critical spacing indicating that the region over which contour interaction occurs is more extensive for children with CVI as compared to normally sighted children. Furthermore, the spread of logMAR visual acuity is much larger in CVI (0.32) than in normally sighted children (.09).

in a child with CVI. G.R. has functional visual acuity, and although he is affected by contour interaction, his visual acuity is not as affected as others with poorer visual acuity.

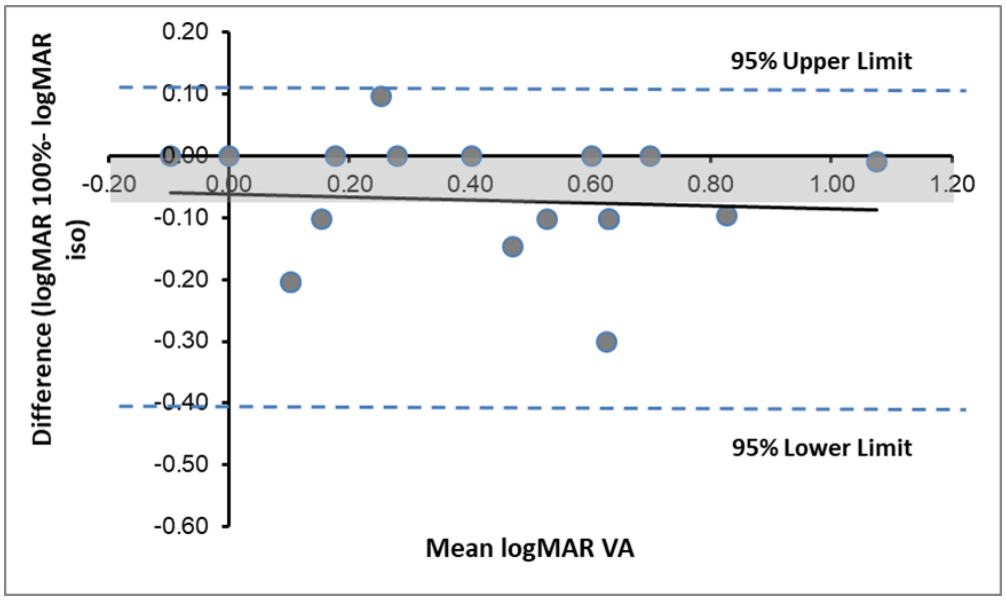

Figure 3.4: Bland-Altman analysis of logMAR 100% versus logMAR isolated for children with CVI.

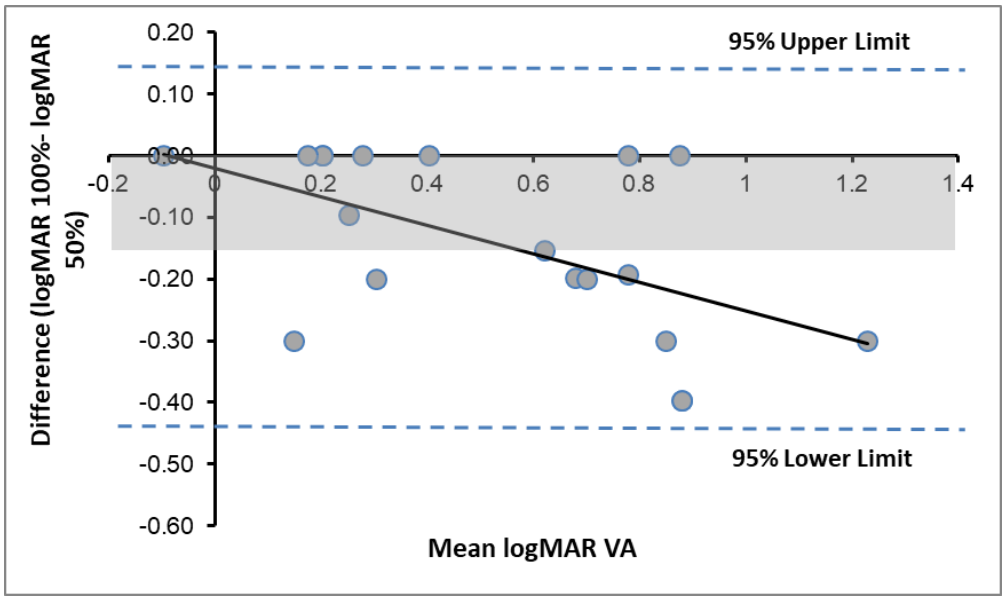

Figure 3.5: Bland-Altman analysis of logMAR 100% versus logMAR 50% for children with CVI.

Case Report 2

B.V. is a 7 year old female who presented for a comprehensive vision exam as a returning patient to the Special Visual Assessment Clinic (SVAC). She was born prematurely at 35

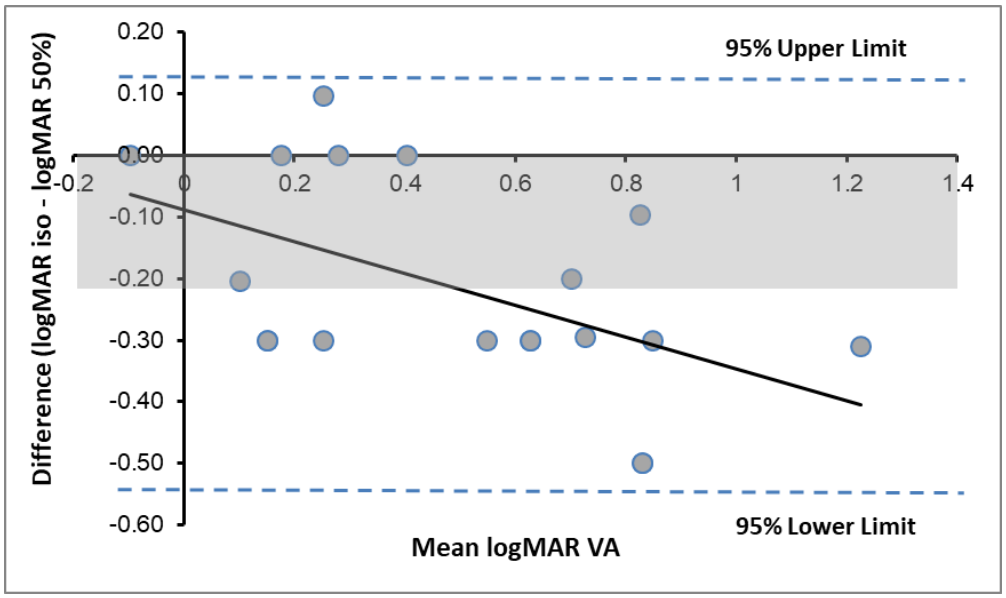

Figure 3.6: Bland-Altman analysis of logMAR isolated versus logMAR 50% for children with CVI.

weeks along with her fraternal twin. Her medical history is significant for cerebral palsy and cerebral visual impairment. Her refractive error is OD +4.00 -1.00 x 180 and OS +4.75 -0.50 x 180. She presents with a 30-40 prism diopter left esotropia. Her Cardiff Acuity Test results show 20/50 visual acuity with her current spectacles. Her logMAR visual acuities for isolated, 100%, and 50% spacing are 0.58 logMAR (20/76), 0.68 logMAR (20/96), and 1.08 logMAR (20/240), respectively. Her Cambridge Contrast sensitivity was mildly reduced to 0.52% and her color vision was normal. Her left esotropia most likely contributes to a visual field restriction to approximately 45 degrees on her left side. B.V. is a good example of how a child with poorer visual acuity with 100% standard spacing with can show significant difficulties in the presence of contour, and that 50% spacing can cause a huge disruption in visual performance (a five lines reduction in visual acuity as compared to an isolated symbol).

These two case reports illustrate that the visual acuity of children with poorer levels of visual acuity show a greater degradation of acuity in the presence of contour interaction. Therefore, it is of utmost importance not to overestimate visual abilities of children with conditions such as CVI so that they may still qualify for vision impairment services through their educational providers.

Discussion

As expected, our findings demonstrate that children with CVI have a larger area over which contour interaction affects visual acuity. This is consistent with previous findings in the literature which demonstrate that children with CVI (specifically PVL) have an elevated crowding ratio (Jacobson et al. 1996). However, there has not yet been a systematic evaluation of the magnitude and extent of critical spacing of contour interaction on visual acuity in children with CVI. For normally sighted children, it is well known that factors other than contour interaction can be considered responsible for the reduction in visual acuity when children read a chart with crowded (linear) optotypes (having one optotype or less spacing between optotypes) (Jacobson et al. 1996). The majority of the CVI population evaluated in this study would have difficulties with being tested with a linear chart for other logistical reasons (head position, non-verbal, intellectual impairment, etc). However, one would expect that a child who is able to perform a linear visual acuity task with CVI may actually be affected more greatly by the spacing of the optotypes presented on a line, unlike a normally sighted child, and it would further be expected that such a child would have a much better single optotype acuity.

As discussed in Chapter 2, these findings may be helpful when making recommendations to teachers and parents. Although standard recommendations for educational purposes tend to focus on print size (and this remains to be important), these findings further elucidate the importance of spacing on visual performance. Both kerning (spacing between characters that may be confused for a different letter e.g. cl and d) and tracking (spacing within an entire word), may need to be adjusted to optimize performance for children with CVI. If standard print is 25% spacing, this certainly is within the realm of contour interaction for children with CVI. In general, children with CVI will need adjusted spacing at about twice that of materials printed for normally sighted children. This estimate seems rather conservative, since it would be expected that flanking letters or optotypes would have an even greater effect than flanking bars on visual acuity and performance. Therefore, double spacing letters may be a good starting point when making recommendations, however, teachers and parents will want to experiment with adjusting spacing as well as print size when finding the optimal parameters for educational materials for each specific child.

Conclusions

The critical spacing for contour interaction in children with CVI is about two times larger than that for normally sighted children. The effects of contour interaction may add to the visual difficulty of a given task for children with CVI. This information may be valuable when making recommendations on print size and spacing in educational materials for children with CVI, as well as general lifestyle recommendations to parents of children with CVI. Further investigation of the effect of flanking optotypes surrounding a central target optotype remains to be done and could further elucidate the real world applicability of these findings.

References

1. Bouma, H. 1970. Interaction Effects in Parafoveal Letter Recognition. Nature 226: 177-78.

2. Coates, Daniel Robert, Jeremy M. Chin, and Susana T.L. Chung. 2013. Factors Affecting Crowded Acuity: Eccentricity and Contrast. Optometry & Vision Science 90 (7): 996-1005.

3. Dutton, G N, E C A McKillop, and S Saidkasimova. 2006. Visual Problems as a Result of Brain Damage in Children. The British Journal of Ophthalmology 90 (8): 932-33.

4. Estes, W. K. 1972. Interactions of Signal and Background Variables in Visual Processing. Perception & Psychophysics 12 (3): 278-86.

5. Fern, Karen D., Ruth E. Manny, James R. Davis, and Roy R. Gibson. 1986. Contour Interaction in the Preschool Child. American Journal of Optometry & Physiological Optics 63 (5): 313-18.

6. Flom, M.C., G.G. Heath, and E. Takahashi. 1963. Contour Interaction and Visual Resolution: Contralateral Effects. Science 142 (3594): 979-80.

7. Flom, Mert. 1991. Contour Interaction and the Crowding Effect. Problems in Optometry 3 (2): 237-57.

8. Good, William V., James E. Jan, S. Burden, A. Skoczenski, and T.R. Candy. 2001. Recent Advances in Cortical Visual Impairment. Developmental Medicine and Child Neurology 43: 56-60.

9. Jacobson, L, U Ek, E Fernell, O Flodmark, and U Broberger. 1996. Visual Impairment in Preterm Children with Periventricular Leukomalacia–Visual, Cognitive and Neuropaediatric Characteristics Related to Cerebral Imaging. Developmental Medicine and Child Neurology 38: 724-35.

10. Jan, J E, M Groenveld, and D P Anderson. 1993. Photophobia and Cortical Visual Impairment. Developmental Medicine and Child Neurology 35 (6): 473-77.

11. Jan, J E, M Groenveld, and A M Sykanda. 1990. Light-Gazing by Visually Impaired Children. Dev Med Child Neurol 32 (9): 755-59.

12. Jan, J E, M Groenveld, A M Sykanda, and C S Hoyt. 1987. Behavioural Characteristics of Children with Permanent Cortical Visual Impairment. Developmental Medicine and Child Neurology 29 (5): 571-76.

13. Kingdom, FAA, and N Prins. 2010. Psychophysics: A Practical Introduction.

14. Legge, Gordon, J. Stephen Mansfield, and Susana T.L. Chung. 2001. Psychophysics of Reading VXX. Linking Letter Recognition to Reading Speed in Central and Peripheral Vision. Vision Research 41 (6): 725-43.

15. Levi, Dennis M. 2008. Crowding–an Essential Bottleneck for Object Recognition: A Mini-Review. Vision Research 48 (5): 635-54.

16. Levi, Dennis M, Srividhya Hariharan, and Stanley A Klein. 2002. Suppressive and Facilitatory Spatial Interactions in Peripheral Vision: Peripheral Crowding Is Neither Size Invariant nor Simple Contrast Masking. Journal of Vision 2 (2): 3.

17. Levi, Dennis M, Shuang Song, and Denis G Pelli. 2007. Amblyopic Reading Is Crowded. Journal of Vision 7 (2): 21.

18. Manny, Ruth E., Karen D. Fern, and David S. Loshin. 1987. Contour Interaction Function in the Preschool Child. American Journal of Optometry & Physiological Optics 64 (9): 686-92.

19. Norgett, Yvonne, and John Siderov. 2014. Foveal Crowding Differs in Children and Adults. Journal of Vision 14 (12): 110.

20. Pelli, Denis G. 2008. Crowding: A Cortical Constraint on Object Recognition. Current Opinion in Neurobiology 18 (4): 445-51.

21. Pelli, Denis G, and Katharine A Tillman. 2008. The Uncrowded Window of Object Recognition. Nature Neuroscience 11 (10): 1129-35.

22. Pelli, Denis G, Katharine A Tillman, J Freeman, Michael Su, Tracey D Berger, and Najib J Majaj. 2007. Crowding and Eccentricity Determine Reading Rate. Journal of Vision 7 (2): 20.

23. Philip, Swetha Sara, and Gordon N Dutton. 2014. Identifying and Characterising Cerebral Visual Impairment in Children: A Review. Clinical Experimental Optometry: Journal of the Australian Optometrical Association 97 (3): 196-208.

24. Pike, MG, G Holmstrom, and LS De Vries. 1994. Patterns of Visual Impairment Associated with Lesions of the Preterm Infant Brain. Developmental Medicine and Child Neurology 36: 849-62.

25. Toet, Alexander, and Dennis M. Levi. 1992. The Two-Dimensional Shape of Spatial Interaction Zones in the Parafovea. Vision Research 32 (7): 1349-57.

Chapter 4

Visual acuity

Background

Overview

Cerebral visual impairment (CVI) is the leading cause of vision loss in children in industrialized nations, and results from an insult to the developing brain. Preferential looking procedures using gratings and the Cardiff picture cards successfully measure visual acuity in non-verbal patients; but both grating acuity and Cardiff cards tend to underestimate the visual acuity reduction associated with amblyopia. It is anticipated that the Cardiff Acuity Test likely would underestimate visual acuity loss in children with CVI due to the lack of contour interaction effects.

As discussed in Chapters 2 and 3, a comparison of two forms of Lea single symbol cards with contour bars was utilized to measure acuity in children with cerebral visual impairment as compared to children with normal vision. In Chapter 2, it was determined that the visual acuity of children with CVI is reduced in the presence of increased contour interaction; this occurs when using cards which have contour bars spaced at 50% of the optotype width away versus 100% of the optotype width away. This effect is not seen in children with normal vision.

In Chapter 3, the extent to which this occurs was evaluated through an analysis of critical spacing. This analysis showed that children with CVI have a critical spacing that is about twice as large as children with normal vision - that is, the extent over which contour had a significant effect on visual acuity is twice as large for children with CVI. This is the framework within which a comparison can now be made to other types of visual acuity testing, as discussed further in this chapter.

Types of Visual Acuity Tests

There are several tests of visual acuity but they measure different aspects of visual resolution and thus are not directly comparable. These include tests of detection (minimum line width equals 0.5 seconds of arc), resolution (minimum resolvable equals 0.5 to 1 minarc), isolated identification (minimum recognizable letter), crowded indentification (minimum recognizable letter with horizontal contour interaction), and hyperacuity or vernier (minimum discriminable offset 3 to 6 secs of arc). The first category of tests for children with various impairments merely assesses the child's ability to detect that something is present. The child is not required to identify or recognize the target of interest. The STYCAR Graded-balls Vision Test, introduced in 1973, was designed to provide visual information from very young children (six months to two and a half years of age) as well as children with various cognitive impairments. The test utilizes two presentations of the test balls either by rolling the balls or mounting them (static presentation by mounting on black sticks). A comparison is made to Snellen equivalence, however, this connection is limited as Snellen is a recognition test (Sheridan 1973) and the STYCAR test may be a test of contrast detection rather than acuity.

Another category of tests is based off the original concepts of forced-choice preferential looking (PL) and the acuity card procedure (Dobson, McDonald, and Teller 1985). This category is defined as resolution tests in which the target must be resolved in some way such as with Teller Acuity Cards. Grating acuity can be measured a number of different ways, but the Teller Acuity Card presentation typically presents a card with a blank gray field on one side and a grating of varying spatial frequency on the other half. If the child is able to resolve the grating, it is expected that the child would attend to the grating rather than the blank gray field. At threshold, both fields appear equally gray. The Teller Acuity Cards were shown to predict normal visual acuity with Snellen charts at age five and a half when testing showed normal responses at age one - conversely, children who did not show high acuity scores with grating at age one continued to have visual difficulties at age five and a half when measured with Snellen charts (Dobson et al. 1999).

The final category includes tests which require a child to recognize the object of interest. One test aimed at obtaining this information in young children is the Kay Picture Test which was a predecessor of the Lea Symbols (Kay 1983). The chart was based off of Snellen sizing and utilizes pictures to create an interesting test for children. Other tests within this category include the Cambridge crowding cards and the Sonksen-Silver Acuity System.

Cardiff Visual Acuity

The Cardiff Test was originally developed with the intention of measuring visual acuity in hard to test groups such as toddlers and young children with intellectual impairment. The test target series includes a single picture target (fish, boat, house, car, train) on a grey

background. Each picture was drawn with a white band bordered by two black bands. If the bands are too narrow to resolve, the picture vanishes into the grey background (Figure 4.2). The original introduction of the test suggested that it showed comparable visual acuity measurements when compared to other accepted visual acuity tests such as the Snellen optotypes, Cambridge, and Teller cards. The advantage of this new test was that it could be administered via preferential looking as needed and was much easier to administer in the toddler age group (Adoh, Woodhouse, and Oduwaiye 1992).

Normative data was established for toddlers ages 12-36 months using the Cardiff Acuity Test. Testing 291 toddlers showed that mean binocular acuity increased from 4.5 to 1.2 min arc, and mean monocular acuity increased from 4.5 to 1.4 min arc over 12-36 months. The data also showed that the inter-ocular difference in acuity estimate was less than 1/3 octave and that binocular acuity was unsurprisingly much easier to obtain (Adoh and Woodhouse 1994).

Comparisons with Cardiff Visual Acuity

The Cardiff Acuity Test was demonstrated to be useful, especially in young toddlers with limited attention. A later study evaluated the effectiveness of the Cardiff Acuity Test in detecting amblyopia as compared to pattern visual evoked potentials (VEP) and the Bailey-Lovie Chart. The Cardiff Acuity Test was only able to identify 5 of the 12 children with amblyopia. As such, this test is not recommended when determining the presence of mild amblyopia (Geer and Westall 1996).

Another study evaluated the use of the Cardiff Acuity Test in identifying significant refractive errors. Sixty-eight children were tested who had known bilateral symmetric refractive error (0.50D of myopia or greater and 1.5D of hyperopia or greater) using both the Cardiff Acuity Test and the Bailey-Lovie Chart. The Cardiff Acuity Test only identified 25% of those with reduced vision due to uncorrected refractive error as compared to 97% with the Bailey-Lovie Chart. Therefore, the conclusion was that reduced acuity caused by uncorrected refractive errors will be underdiagnosed when only the Cardiff Acuity Test is used (Howard and Firth 2006).

A comparison of Teller Acuity Cards and Cardiff Acuity Cards in children below the age of two also found that the acuity reduction due to significant refractive errors were missed more often with Cardiff than with Teller. They recommended that the Cardiff test can be useful and "child-friendly," however, care must be taken not to miss visually significant ocular issues (Sharma et al. 2003).

Children with multiple disabilities were evaluated using VEP and Keeler or Cardiff acuity cards. This study found that it was more challenging to be successful with visual acuity cards as compared to VEP, however, the VEP and acuity card thresholds were significantly

correlated. In children with very poor vision, the VEP was found to give better visual acuity readings (Mackie et al. 1995).

Predicted versus Measured Cardiff Visual Acuity

Our extensive clinical testing on both normally sighted and visually impaired children has allowed our lab to utilize a nomogram for determining predicted letter acuity based on measured grating visual acuity. The equation is as follows:

$$MAR(optotype) = [MARgrating - 1/0.4] * 1.3 + 1$$

This adjustment may provide better agreement between the two visual acuity tests as demonstrated in this study.

Study

Purpose

Preferential looking procedures using gratings and the Cardiff picture cards successfully measure visual acuity in non-verbal patients; but both grating acuity and Cardiff cards tend to underestimate the visual acuity reduction associated with amblyopia. It is anticipated that Cardiff cards would also underestimate visual acuity loss in children with CVI due to the lack of contour interaction of the target. Visual acuity, measured with Cardiff cards and Lea symbols that had contour bars at 100% and 50% spacing, was evaluated through a retrospective, observational clinical study. The goal of the study was to determine if a different preferential looking procedure may give more information in children with CVI regarding visual acuity. If so, it may be recommended to eye care providers to utilize different preferential looking cards when measuring visual acuity in this population.

Methods

Binocular visual acuity was measured during a comprehensive vision examination of 15 children (ages 4-18 years; mean 8.6 years) presenting with a diagnosis of CVI (etiologies listed in Table 4.1). Single Lea symbols with contour flanker bars at 50% and 100% spacing were presented in a two-alternative forced choice task using the apple and the house as the test optotypes. Binocular visual acuity was measured with the Cardiff Visual Acuity Test which required detection of an isolated shape on a grey background. Visual acuity thresholds were determined using the modified acuity card procedure by observation of the child's eye gaze, pointing, and/or naming of the optotype. The majority of children with CVI tested in this study population were non-verbal or had limited verbal skills, and therefore, eye gaze was often the only method possible.

Etiology	Number of Subjects
Hydrocephalus	1
Microcephaly	1
Periventricular leukomalacia (white matter damage)	4
Joubert Syndrome	2
Hypoxic Ischemic Encephalopathy/cerebrovascular accident/birth trauma	1
Confirmed diagnosis of CVI, unspecified	2
Infection/drug exposure in utero	1
Injury/malformation of corpus callosum	1
Cerebellar hypoplasia/atrophy	1
Unclear etiology, risk of CVI based on history	8

Table 4.1: Etiologies of CVI subject pool.

Cardiff VA logMAR	logMAR 100%	logMAR 50%
0.50	0.78	0.98
0.00	0.20	0.40
0.40	0.70	0.88
0.00	0.23	0.23
0.30	0.81	0.10
0.60	1.18	1.38
0.60	0.90	1.20
0.50	0.70	0.88
0.30	0.90	1.10
0.57	0.90	1.20
0.60	1.10	1.10
0.30	0.58	0.78
0.10	0.60	0.60
0.00	0.00	0.30
0.63	1.08	1.38

Table 4.2: Raw data for children with CVI. Visual acuity is listed in logMAR values.

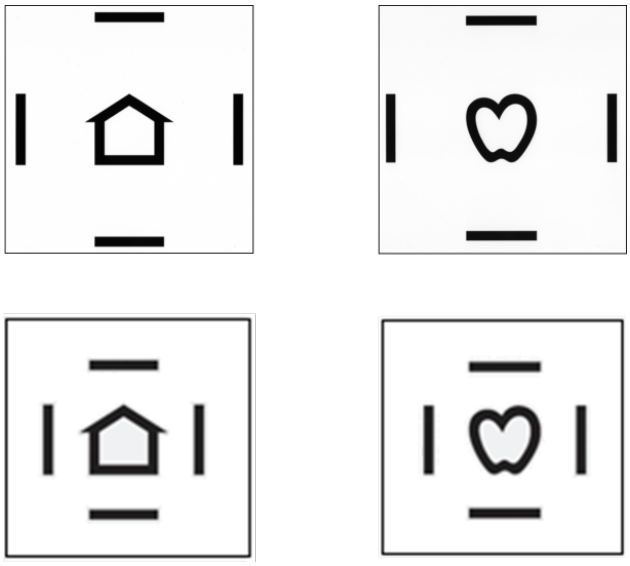

Figure 4.1: Example of 100% and 50% spacing around two Lea optotypes, presented in two alternative forced choice manner.

Figure 4.2: Example of the Cardiff acuity card; the shape is located either at the top or bottom of the grey background.

Results

For this study group, the ranges for visual acuity were found to be Cardiff logMAR 0 to 0.6 (Snellen equivalent 20/20 to 20/80). For the Lea 100% spacing test, the ranges were logMAR

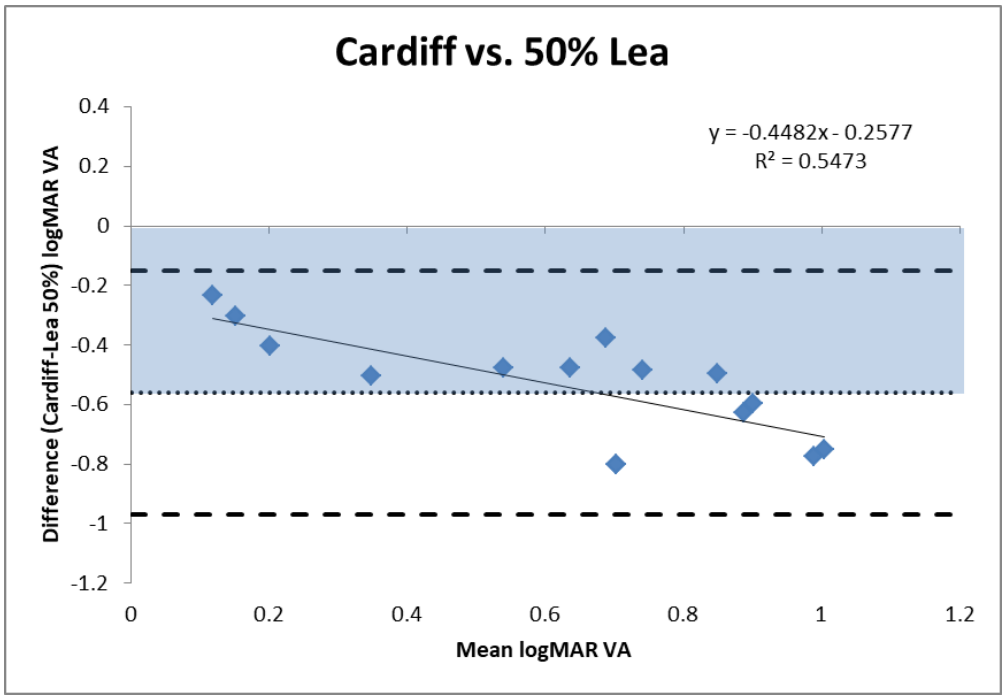

Figure 4.3: Bland-Altman plot of the difference between Cardiff acuity and 50% Lea cards versus mean visual acuity. This demonstrates the largest discrepancy between two measures performed. The Cardiff Acuity Test underestimated vision loss by over 5 lines (0.54 logMAR) when compared to the 50% Lea visual acuity. Furthermore, the slope indicates a downward trend which shows that as visual acuity worsens, the difference between two measures increases. Thus, it is more likely to underestimate vision loss for a child with greater visual impairment if only testing with the Cardiff Acuity Test.

0 to 1.18 (Snellen equivalent 20/20 to 20/300). The lowest acuity ranges were found with Lea 50% spacing and were found to be logMAR 0.23 to 1.38 (Snellen equivalent 20/32 to 20/500). Cardiff visual acuity was generally better than either Lea 100% spacing or Lea 50% spacing for most subjects. Using the equation to predict optotype acuity listed above, the Cardiff acuity range was logMAR 0-1.06 (Snellen equivalent 20/20 to 20/230).

Bland-Altman analysis is utilized to describe the differences between two measures. It plots the mean versus the difference between two measures. A Bland-Altman analysis comparing Cardiff visual acuity to the 100% and 50% spacing Lea visual acuity was performed. When compared to Lea 50% spacing cards, Cardiff acuity underestimates the average vision loss by -0.54 logMAR, and this difference increases with worse acuity. The slope is significantly different from zero at $p < .01$ ($p = .008$). This is equivalent to about 5.5 lines (for example, 20/20 versus 20/63 would be a five line difference on a log based visual acuity chart). A similar analysis was performed with the adjusted Cardiff measurements as compared to 50%

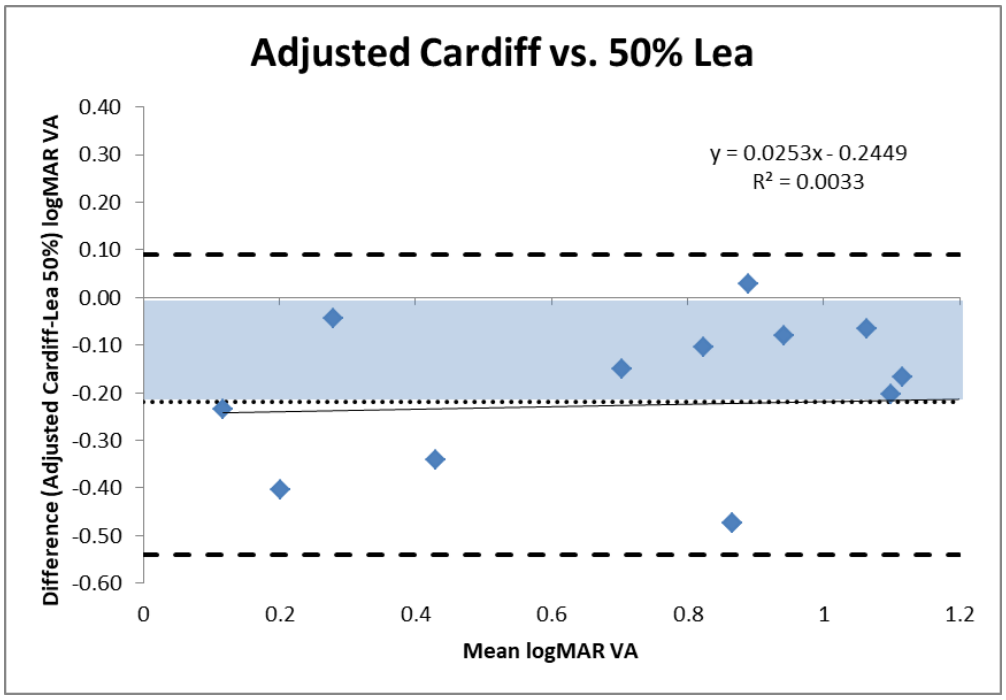

Figure 4.4: Bland-Altman plot of the difference between adjusted Cardiff acuity and 50% Lea cards versus mean visual acuity. This demonstrates a much smaller discrepancy of only about two lines. The Cardiff Acuity Test underestimated vision loss by 2 lines (0.22 logMAR) when compared to the 50% Lea visual acuity.

Lea visual acuity, and the difference was found to be much smaller at -0.22 logMAR in this case (two line difference). This slope was not found to be significantly different from zero.

A similar analysis was performed to compare Cardiff visual acuity and 100% Lea visual acuity. Cardiff visual acuity underestimates vision loss by -0.35 logMAR, and this difference increases with worse acuity. The slope is significantly different from zero at $p < .05$ ($p = .037$). This is not as large of a difference, but still accounts for about 3.5 lines of visual acuity difference on a log based visual acuity chart (for example 20/20 versus 20/50). As with the 50% spacing, another analysis was performed with the adjusted Cardiff measurements as compared to 100% Lea visual acuity, and the difference was also found to be much smaller at -0.04 logMAR in this case (less than half a line difference). This slope was also not found to be significantly different from zero.

Similar to the analysis performed in Chapter 2, the 50% Lea visual acuity and 100% Lea visual acuity were compared with a Bland-Altman analysis. The difference between the two measures was found to be -0.16 logMAR, or the equivalence of about a line and a half. In this case, the slope was not significantly different from zero at $p = 0.36$. This is consistent with

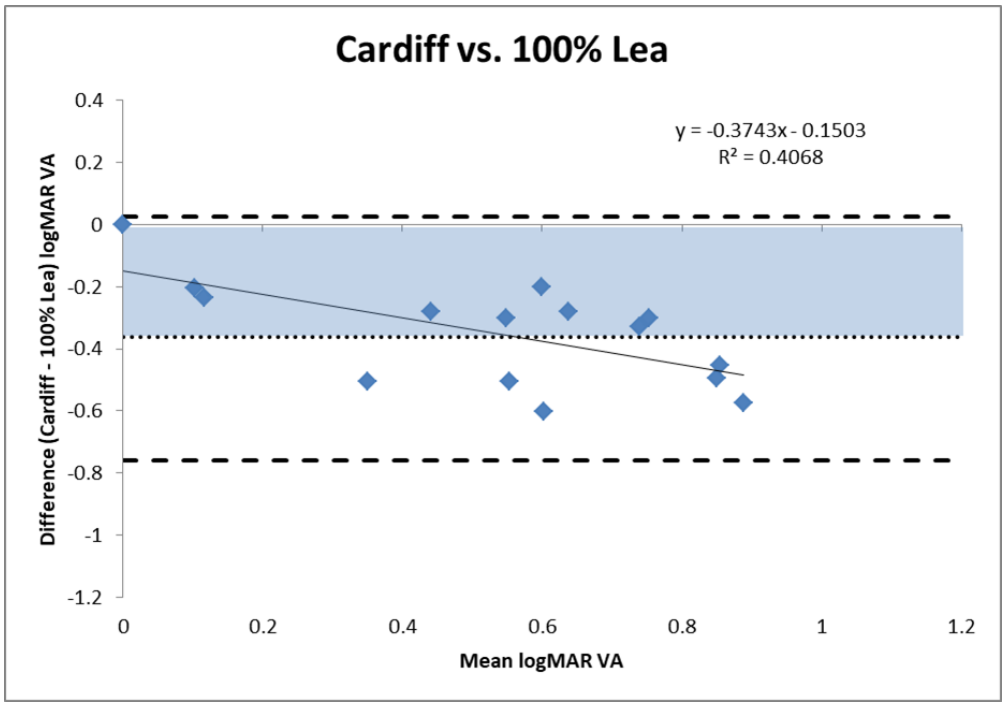

Figure 4.5: Bland-Altman plot of the difference between Cardiff and 100% Lea versus mean visual acuity. This also shows a discrepancy between measures, although it is shown to be smaller (over three line difference). Once again, the downward slope indicates that the difference between measures increases with worse visual acuity.

the trend seen in Chapter 2, although the Chapter 2 results were found to be significant, possibly due to a much larger sample size.

When compared to both measures, Cardiff visual acuity underestimated the vision loss compared to 100% and 50% spacing Lea visual acuity, and the disparity between measures was worse for 50% spacing as well as for children with worse visual acuity. This is indicated by the slope of the graph - as the visual acuity worsens, the difference between the two measures increases. However, when using the adjusted Cardiff values according to our equation, the difference between measures was much smaller indicating that Cardiff measurements may be more reliable in children with CVI if they are adjusted.

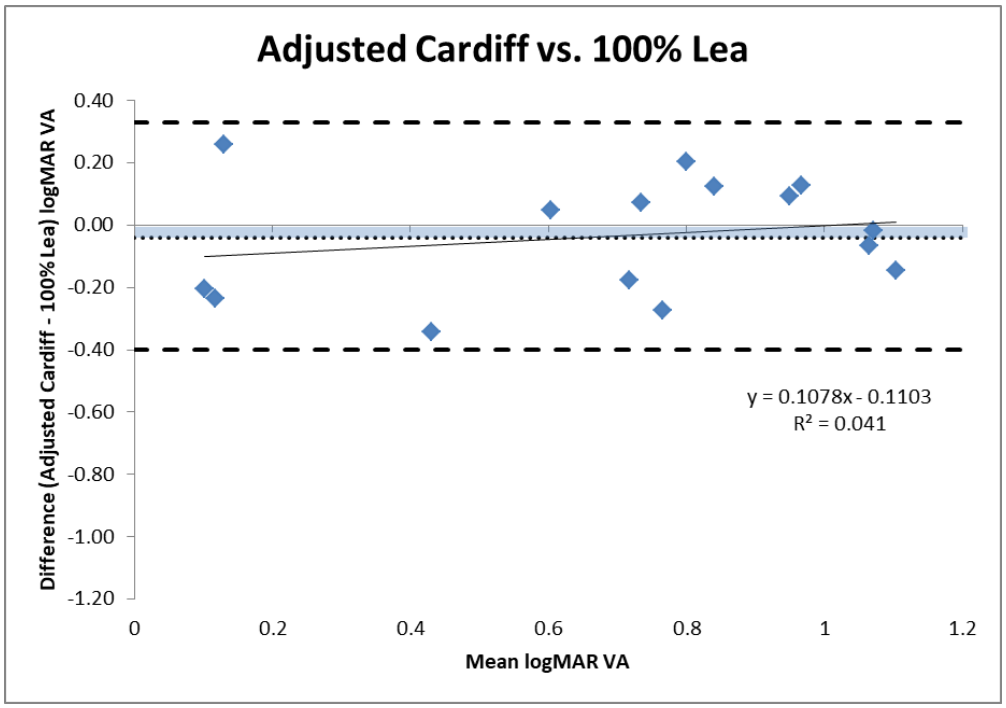

Figure 4.6: Bland-Altman plot of the difference between adjusted Cardiff and 100% Lea versus mean visual acuity. This shows a much smaller difference between measures at less than half a line (0.04 logMAR).

Example Case Discussion

One case report shows quite dramatically the risk of underestimating vision loss when using the Cardiff Acuity Test, as compared to a more challenging method such as 100% or 50% Lea symbols.

T.B. is an 18 year old male who presented for a comprehensive eye exam to the Special Visual Assessment Clinic (SVAC). His medical history is significant for cerebral visual impairment secondary to microcephaly. He also has been diagnosed with cerebral palsy and hypotonia. He has a history of bilateral cataracts for which he underwent cataract extraction followed by YAG capsulotomy for secondary posterior subcapsular cataract formation. His vision is corrected with OD +0.50 DS and OS +1.50 DS with a +3.00 add in progressive addition lenses. He also presents with a small alternating esotropia that is more often present in the left eye. His Cardiff Acuity Test visual acuity was measured to be 20/80 (logMAR 0.60) with both eyes viewing. Using our conversion factor, our predicted letter acuity at this level is 20/215. When measured with Lea 100% and Lea 50% his visual acuity was 20/300 (logMAR 1.18) and 20/480 (logMAR 1.38) respectively. The predicted visual acuity of 20/215 from the 20/80 Cardiff measure does not fully demonstrate the level to which the CVI affects the

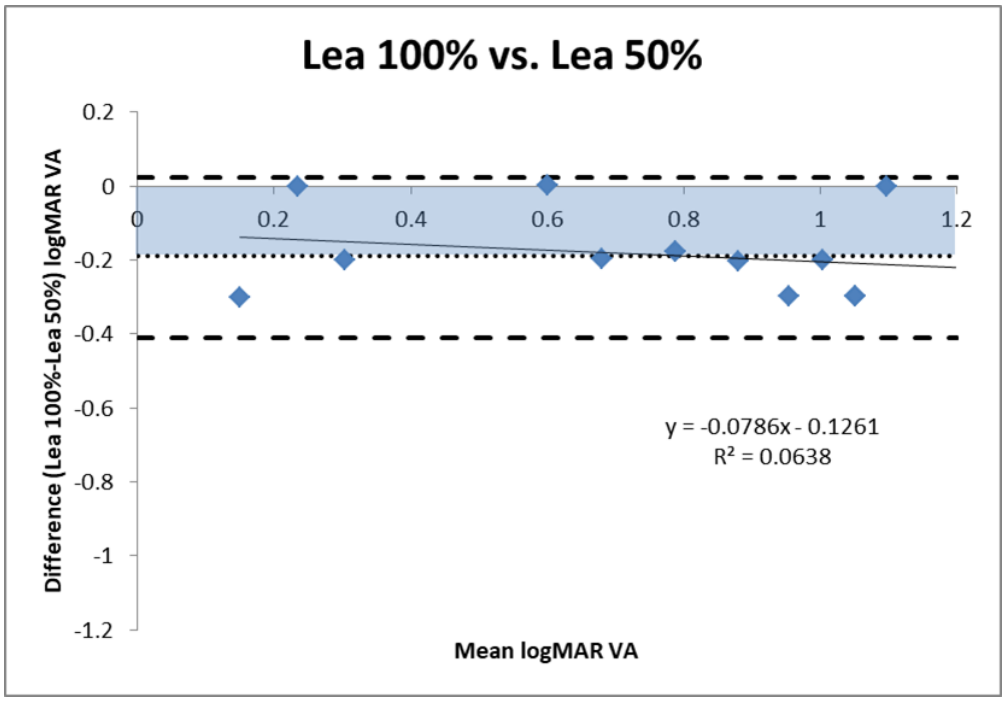

Figure 4.7: Bland-Altman plot of the difference between 50% and 100% Lea versus mean visual acuity. This trend is consistent with the results from Chapter 2 in which visual acuity tended to be worse (or the same for three subjects) with 50% Lea symbols as compared to 100% Lea symbols. It also shows a similar pattern in which the difference between the two measurements increases with worse acuity.

visual function and performance but is a better estimate than the uncorrected Cardiff acuity value. It is of utmost importance not to underestimate the level of vision loss so there are not unrealistic expectations placed on children, and so that they still may continue to qualify for low vision services.

Discussion

The Cardiff Acuity Test is a quick and easy-to-administer clinical test for obtaining visual acuity in young children or children who are non-verbal. As other studies have shown, the Cardiff Acuity Test can be helpful when measuring vision in normally sighted children. However, when children present with some other condition such as amblyopia, high refractive error, or in the case of this study, CVI, the Cardiff Acuity Test has a tendency to significantly overestimate the visual acuity (or underestimate the amount of true loss caused by the visual impairment).

Cardiff Acuity underestimates vision loss by three to five lines on average when compared to the flanked Lea symbols. Furthermore, children with poorer vision had an even greater disparity between the Cardiff and Lea measurements. This is particularly concerning since children who may have significant impairments may not be identified as having severe visual impairment. One study evaluated ways to improve the reliability of visual acuity tests in children - they showed that logarithmic progression of optotype size, such as with Lea symbols but not with Cardiff Acuity, offers improvements in test performance in terms of sensitivity as well as reliability (McGraw et al. 2000). When adjustments were made to the Cardiff measurement using our equation, the agreement between the two measures was much closer. This indicates that it may be best to adjust the Cardiff measurements, especially in children with CVI to more closely resemble the true visual performance of the child.

The main advantages of the Cardiff Acuity Test are the ease of administering the test, as well as the advantage that it may be performed as a preferential looking test. However, there are disadvantages to overestimating visual acuity in children with visual impairment, especially in the case of CVI. It can be challenging to obtain services for children with CVI, especially if their visual performance is closer to expected age and academic level. As a result, children who are measured with a test that may be too easy can lose out on the opportunity to obtain services through their school district for educational success. Educational interventions can be especially important for individuals within the CVI population since some individuals will also be at a higher risk for learning disabilities (Litt et al. 2005). Furthermore, identification of an optotype is a more challenging task than detection. Detection can be important for safe movement throughout the world, but it does not easily translate to functionality in classroom settings or with independent living skills. As a result, it is recommended that more than one measurement of visual acuity be utilized in children with CVI to determine the breadth and range of vision function, and to provide the tools to advocate for additional services for the child as needed. If practitioners choose to utilize the Cardiff test for children with CVI, they may consider adjusting the result to get a closer to prediction to the child's true visual performance. Finally, a more standardized visual acuity task such as the Lea symbols may provide a good option for practitioners interested in assessing the wide and variable range of visual function in children with CVI.

Conclusions

For 93% of the patients with CVI, 50% and 100% Lea symbols yielded a more reduced acuity compared to the Cardiff Acuity Test, unless the Cardiff results were adjusted; the latter only requires detection of the symbols, whereas the Lea symbols require discrimination between an apple and a house optotype.

The Cardiff Acuity Test is a useful clinical tool and can be applied to many situations. However, it may not be the ideal visual acuity test for children with CVI, as underestimating the amount of vision loss could make it challenging to obtain services for an already widely misunderstood visual condition. If utilized, we suggest that the measurements be adjusted to account for the difference in difficulty between identification and detection. This also further highlights the importance of not simply relying on one test when assessing vision, especially in individuals with visual impairment.

Reporting visual acuity in the presence of contour interaction in children with CVI would be helpful when making educational recommendations to the child's parents and care team, and this ultimately may be a preferred method for measuring children with CVI by private practitioners and researchers alike.

References

1. Adoh, Tonnie O., and J. Margaret Woodhouse. 1994. The Cardiff Acuity Test Used for Measuring Visual Acuity Development in Toddlers. Vision Research 34 (4): 555-60.

2. Adoh, Tonnie O., J.M. Woodhouse, and K.A. Oduwaiye. 1992. The Cardiff Test: A New Visual Acuity Test for Toddlers and Children with Intellectual Impairment. A Preliminary Report. Optometry & Vision Science 69 (6): 427-32.

3. Dobson, Velma, Mary Alice McDonald, and Davida Y Teller. 1985. Visual Acuity of Infants and Young Children: Forced-Choice Preferential Looking Procedures. American Orthoptic Journal 35 (1). Taylor & Francis: 118-25.

4. Dobson, Velma, Graham E. Quinn, R. Michael Siatkowski, John D. Baker, Robert J. Hardy, James D. Reynolds, Michael T. Trese, and Betty Tung. 1999. Agreement between Grating Acuity at Age 1 Year and Snellen Acuity at Age 5.5 Years in the Preterm Child. Investigative Ophthalmology and Visual Science 40 (2): 496-503.

5. Geer, Indira, and Carol A. Westall. 1996. A Comparison of Tests to Determine Acuity Deficits in Children with Amblyopia. Ophthalmic and Physiological Optics 16 (5): 367-74.

6. Howard, Claire, and Alison Y. Firth. 2006. Is the Cardiff Acuity Test Effective in Detecting Refractive Errors in Children? Optometry and Vision Science 83 (8): 577-82.

7. Kay, Hazel. 1983. New Method of Assessing Visual Acuity with Pictures. British Journal of Opthalmology 67: 131-33.

8. Litt, Jonathan, H Gerry Taylor, Nancy Klein, and Maureen Hack. 2005. Learning Disabilities in Children with Very Low Birthweight: And Educational Interventions. Journal of Learning Disabilities 38 (2): 130-41.

9. Mackie, R. T., D. L. Mc Culloch, K. J. Saunders, J. Ballantyne, R. E. Day, M. S. Bradnam, and G. N. Dutton. 1995. Comparison of Visual Assessment Tests in Multiply Handicapped Children. Eye (Basingstoke) 9 (1): 136-41.

10. McGraw, Paul V., Barry Winn, Lyle S. Gray, and David B. Elliott. 2000. Improving the Reliability of Visual Acuity Measures in Young Children. Ophthalmic and Physiological Optics 20 (3): 173-84.

11. Sharma, P, D Bairagi, M M Sachdeva, K Kaur, S Khokhar, and R Saxena. 2003. Comparative Evaluation of Teller and Cardiff Acuity Tests in Normals and Unilateral Amblyopes in Under-Two-Year-Olds. Indian Journal of Ophthalmology 51 (4): 341-45.

12. Sheridan, Mary D. 1973. The STYCAR Graded-balls Vision Test. Developmental Medicine & Child Neurology 15 (4): 423-32.

Chapter 5

Contrast sensitivity

Background

Patients with cerebral visual impairment (CVI) have vision loss resulting from an insult to the brain rather than to ocular structures. CVI can be characterized by unique behaviors that may extend beyond basic visual functions such as visual acuity. CVI is the result of damage that occurs to the retrogeniculate visual pathway and hypoxic brain injury is the most common etiology of CVI (Afshari, Afshari, and Fulton 2001). Other common etiologies include prematurity, hydrocephalus, structural central nervous system abnormalities, and seizures (Khetpal and Donahue 2007). One of the affected visual functions in children with CVI is loss of contrast sensitivity, although this does not always mirror the level of visual acuity loss (Philip and Dutton 2014). It is well established that visual acuity is not the only important factor when determining visual function. In fact, other methods such as the Smith-Kettlewell Institute Low Luminance (SKILL) Card, demonstrate the effects of reduced luminance and contrast on visual acuity, highlighting the interactions of various visual functions (Haegerström-Portnoy et al. 1997). To understand how contrast sensitivity is reduced in children with CVI, it is helpful to understand what is expected with respect to contrast sensitivity in normally sighted children.

Contrast Sensitivity Development in Children

The longstanding theory regarding contrast sensitivity in children was that they did not attain adult levels of visual sensitivity until their teenage years (Slataper 1950; Weymouth 1963). In 1982, Bradley and Freeman published a study showing that methodology may have been the limiting factor in previous studies. They found that children 3.5 years of age and older had a mean contrast sensitivity 0.35 log units lower than adults (less than previously reported). They also reported a gradual increase in contrast sensitivity with age, reaching near adult levels around eight years of age (Bradley, Arthur and Freeman 1982).

It is well established that contrast sensitivity in human infants improves with age based on

objective measurements (Salapatek and Banks 1978). Behavioral studies show a similar improvement in contrast sensitivity, with a shift in peak contrast sensitivity between 4 months and 4 years of age (Gwiazda et al. 1997).

A more recent review by Leat et al. 2009, found that contrast sensitivity can mature fully between 8 and 19 years depending on the method used. This is quite a large range of ages for such an important visual function to show full development. The following table summarizes the conclusions of the studies reviewed by Leat. It appears that method of measurement has the largest impact on the result of these studies (Leat, Yadav, and Irving 2009).

Study	Result
Atkinson, French, and Braddick 1981	There is a difference between 4 year olds and adults.
Derefeldt, Lennerstrand, and Lundh 1979	There is no difference between 6-10 year olds and adults.
Ellemberg et al. 1999	CS adult-like by 7 years but not by 6 years.
Benedek et al. 2003	There is a difference between 5-6 year olds and 9-10 year olds, and between 9-10 year olds and 11-12 year olds.
Abramov et al. 1984	There is a difference between 6-8 year olds and adults of 0.3 log units.
Scharre et al. 1990	CS is not adult-like by 7 years.
Leat and Wegmann 2004	CS is not adult-like by 6-8 years.
Gwiazda et al. 1997	CS is not adult-like by 8 years.
Norcia, Tyler, and Hamer 1990	Between 4 and 9 weeks, CS increased by a factor of 4-5 at all spatial frequencies.
Banks and Salapatek 1975	Limited range of spatial information available to the infant.
Bradley, Arthur, and Freeman 1982	CS is near adult levels around 8 years.

Table 5.1: Summary of studies on contrast sensitivity in pediatric populations adapted from Leat 2009.

Contrast Sensitivity in CVI

Visual acuity has been shown not to be the best predictor for other measures of spatial vision (Haegerström-Portnoy et al. 2000). Previous studies examining other low vision conditions such as glaucoma and retinal disease have shown a dissociation between visual acuity and contrast sensitivity measurements. That is, while contrast sensitivity and visual acuity mea-

surements correspond well in normally sighted individuals, this is typically not the case in individuals with low vision (Atkin et al. 1979; Wolkstein, Atkin, and Bodis-Wollner 1980).

Others suggest there may be a more apparent predictable pattern in low vision when analyzing the contrast sensitivity function. Chung and Legge (2016) found that there was a predictable shift along the log-spatial frequency and log-contrast sensitivity axes that could account for the level of impaired acuity and contrast sensitivity in individuals with low vision due to retinal or nerve disease (Chung and Legge 2016). That is, they were able to demonstrate a predictable shift of the normal contrast sensitivity function in low vision subjects.

There is no clear consensus on how contrast sensitivity is affected in individuals with CVI. One study examining patients with periventricular leukomalacia found that contrast sensitivity was not often affected (Jacobson et al. 1996) - however, in a CVI review by William Good, he references the possibility of deficits in contrast sensitivity in children with CVI (Good et al., 2001).

Cambridge Low Contrast Gratings

In the 1980s, measurement of threshold contrast with gratings and stripes became a technique that received much attention. One study evaluated the sensitivity of the visual system to gratings at threshold contrast in a group of patients with diabetes. Out of this study, the Cambridge Low Contrast Gratings Test was developed; and in this initial study the researchers reported excellent test-retest reliability (Della Sala et al. 1985).

A later iteration of this original idea was introduced in 1988. The goal was to develop a procedure that would test contrast sensitivity at a spatial frequency close to the maximum sensitivity of the normal human visual system. It was also designed to eliminate ceiling and floor effects that can occur with other tests of contrast sensitivity. Another original intention of the test was to study populations of patients with various conditions including diabetes, multiple sclerosis, optic neuritis, and glaucoma. Their data suggests that from age twenty onward, the contrast sensitivity scores for normally sighted individuals decreases by about 10% for each decade of life. As such, it was suggested that it may be a more useful test in studying younger rather than older populations. One of the advantages for the study of the population of interest with CVI, is that the Cambridge Low Contrast Gratings test allows for a two-alternative forced choice manner of testing (Wilkins et al. 1988).

Adult levels for contrast sensitivity were reached in normally sighted children with this test after age 10 years, with an age-dependent improvement. In the same study, children with developmental delay were found to have a significantly lower score when compared to normal children (Nielsen et al. 2007a).

Other groups evaluated the reliability of the Cambridge Low Contrast Gratings and found

a large performance range for subjects (all adults). The recommendation was therefore to avoid using the Cambridge Gratings for screening eye disease (Jones, Moseley, and Thompson 1994). In another study, researchers evaluated the usage of the Cambridge Low Contrast Gratings Test in children, specifically those with developmental delay. This group found a significantly lower score in children with developmental delay compared to normal children (t=2.66, P=0.022). They further emphasized the usefulness of the test in preschool children and children with developmental delay due to its simplicity (Nielsen et al. 2007b).

The data on Cambridge Low Contrast Gratings test scores in children with CVI is limited. One study analyzed the visual functions of very preterm babies (CVI/PVL risk) and found the median contrast sensitivity score was significant lower than the term controls (190 and 210 for left and right eyes of preterm children versus 250 for each eye of normal children, $p<0.001$) (Cooke 2004).

Relationship Between Contour Interaction and Contrast Sensitivity

Although there continues to be disagreement about contrast sensitivity reduction in children with CVI, some children with CVI will often exhibit a reduction in contrast sensitivity (Good, Hou, and Norcia 2012). Furthermore, we know that contrast sensitivity is vital to functional vision and is often a better predictor of visual functions such as mobility (Marron and Bailey 1982) and face recognition (Owsley and Sloane 1987), as well as quality of life (Bansback et al. 2007). Studies in normally sighted individuals have shown that the crowding effect is reduced for low contrast letters as compared to high contrast letters when viewed foveally (Kothe and Regan 1990). In addition, critical spacing has been shown to become smaller for low-contrast targets, more so in the retinal periphery than in the fovea in normally sighted individuals (Coates, Chin, and Chung 2013). If these results hold for children with CVI, then a potential way to reduce the effect of crowding is to reduce the contrast of an object and its background. However, given the contrast deficits of some children with CVI, reducing the contrast of objects may not be effective. One area that remains to be explored is to directly analyze contour interaction with low contrast targets and flankers. Quantification of this finding in children with CVI could lead to a better understanding of functional vision in light of more realistic conditions; that is, visual conditions of varying contrast which often more closely mimic real-world situations.

It is well established within the crowding literature that adjacent objects can reduce the ability to identify an object without overlapping flankers. In peripheral vision, this has been demonstrated to occur over large distances (Bouma 1970; Toet and Levi 1992; Levi, Hariharan, and Klein 2002). Masking describes overlapping flankers which can reduce the discriminability of a target (Legge and Foley 1980; Foley 1994). This brings up the question of whether crowding is simply a form of masking with flanks that are more remote (Chung, Levi, and Legge 2001). However, the two phenomena are difficult to compare. The general

consensus is that the phenomenon is different when it occurs at the fovea rather than in the peripheral. In the fovea, except at the resolution limit (Danilova and Bondarko 2007), limitations can be attributed to contrast masking. In the periphery, the magnitude and extent of crowding is much greater than the extent of masking (Levi, Hariharan, and Klein 2002), and it is therefore widely accepted that peripheral crowding is not due to simple contrast masking.

Functional Implications of Contrast Sensitivity Loss

Studies within the low vision literature have long considered contrast sensitivity to be an extremely important indicator of visual function. One simulated cataract study evaluated the effects of cataract on clinical and real world vision, and they determined that contrast sensitivity and glare were better representatives of patient vision than visual acuity (Elliott et al. 1996). In fact, it is well accepted that reduction in spatial vision, such as reduced contrast and luminance, with age causes significant impairment in a large portion of elderly patients (Haegerström-Portnoy, Schneck, and Brabyn 1999). Studies in infants indicate that the contrast sensitivity function is limited and continues to expand with age. If the ability to perceive contrast across a range of spatial frequencies (or contrast sensitivity function - CSF) were to remain underdeveloped, as it is in infancy and early childhood, it could have a significant impact on visual function (Banks and Salapatek 1976).

Amblyopia as an Analogous Model

Much of our understanding of the relationship between contrast sensitivity and contour interaction comes from studies in individuals with amblyopia. Other studies have shown that the crowding ratio (visual acuity of single optotypes compared to a line of optotypes) for high contrast letters (96% contrast) is significantly higher than low contrast letters (11% contrast), and that the crowding effect is only apparent for high contrast optotypes ($t=2.03$, $p<0.05$) (Simmers et al. 1999). Crowding has also been shown to be contrast dependent in some unilateral amblyopic eyes of both children and adults; this exemplifies the strength of crowding in these groups (Giaschi et al. 1993).

Research in amblyopia has shown that there are two main areas of deficit in visual performance related to visual acuity and to contrast sensitivity. Non-binocular observers with mild-to-moderate acuity loss have better monocular contrast sensitivity than binocular observers with the same level of visual acuity loss. Furthermore, non-binocular individuals typically have a worse optotype and Vernier acuity than those with residual binocularity (McKee, Levi, and Movshon 2003).

Contrast sensitivity has an important role in visual function in amblyopia. Monocular contrast deprivation has been identified as one of the causal agents in anisometropic amblyopia (Bradley and Freeman 2018). In another study, the contrast sensitivity function of children

with amblyopia was evaluated and a linear relationship was drawn between the contrast sensitivity function and visual acuity of the amblyopic eye. However, after treatment with patching therapy, the visual acuity difference between eyes declined but the contrast sensitivity function remained reduced in the amblyopic eye (Rogers, Bremer, and Leguire 1987).

Public Health Impact

As discussed before, CVI is the leading cause of bilateral visual impairment in children in western countries (Good et al. 2001). Many individuals stand to benefit from improved measurements as well as a more thorough understanding of how visual functions are affected by this condition. Researchers who work with low vision populations have long appreciated the value of contrast sensitivity measurements when determining visual function of a patient. The Cambridge Low Contrast Grating Test is a measure of peak contrast sensitivity, but others have found that even low contrast acuity can be useful as a test of visual function (Regan and Neima 1983). Visual function is an important indicator of quality of life - therefore, many individuals stand to gain an improvement in quality of life with a better understanding of contrast sensitivity function.

Study

Methods

Thirty children with a diagnosis of cerebral visual impairment (CVI) participated during a comprehensive vision examination at the Special Visual Assessment Clinic (SVAC). The group was composed of 15 females and 15 males ages 3-20 with a mean age of 9.17 years. The study protocol was approved by the Institutional Review Board and followed the tenets of the Declaration of Helsinki. Visual examination included evaluation of anterior and posterior segments as well as retinoscopy and visual functions assessment. Threshold visual acuity was measured using the apple and house Lea symbol optotypes with four flanking bars in a two-alternative forced choice task with edge-to-edge (optotype to flanking bar) spacings of 50% and 100% times the optotype width (commercially available, GoodLite). Both optotypes and flanking bars were at 100% contrast level. The subjects were tested with both eyes open during their comprehensive eye examination with best spectacle correction in place. Most subjects were tested with Lea symbols at 1 meter, but if unable to perform the task, the test distance was moved closer to 50 centimeters. Rewards for responses were given as needed (stickers or Cheerios). Peak contrast sensitivity was also measured in the same visit using the Cambridge Low Contrast Grating Test in a two alternative forced choice task (Figure 5.1). Cambridge testing was performed primarily at 1.5 meters. The Cambridge tests contrast sensitivity at a spatial frequency of 4 cycles/degree. Modified acuity card procedures were used and subjects had to demonstrate 75% correct responses to receive credit for reaching a particular visual acuity or contrast level. Fifteen normally sighted children were also selected from the Pediatric Clinic population. This group was composed of 5 males and 10 females

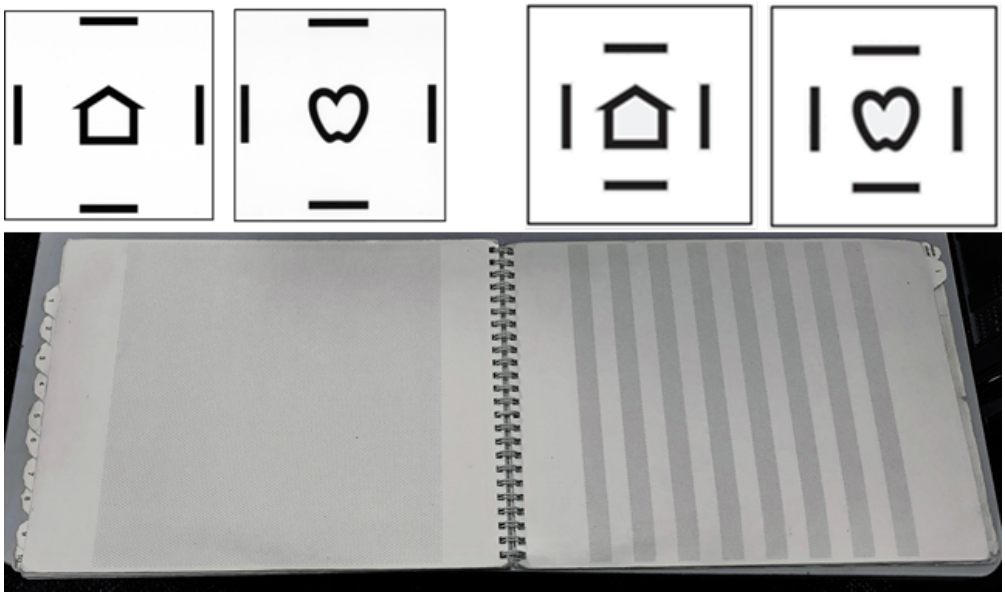

Figure 5.1: Example of VA targets with 100% and 50% spacing of the flanking bars and the Lea symbols, presented as a two-alternative forced choice. Cambridge Low Contrast Grating Test shown on the bottom.

aged 4-10 years with a mean age of 6.3 years. The same visual examination protocol was used, including threshold visual acuity measurements with Lea optotypes with flanking bars at 50% and 100%. The subjects were tested with both eyes open with their best spectacle correction in place. None of the fifteen subjects had any eye disease or vision issues, with the exception of correctable low refractive error.

Results

Visual acuity was measured in all subjects with CVI. Visual acuity ranged from -0.10 logMAR to 1.38 logMAR. Worse visual acuity with 50% spacing was found in all subjects but four who had no difference between the 50% and 100% visual acuity measurements. Contrast sensitivity ranged from 0.19% to 3.2% (average 0.78%) in children with CVI. As expected, there is a positive correlation between visual acuity and contrast sensitivity (Figures 4.2 and 4.3). This means that as visual acuity improves, contrast sensitivity also tends to improve. Furthermore, it is worth nothing that this group of subjects with CVI had contrast sensitivity values that were quite good. It is worth noting that a wider range often shows a decent correlation. However, the relationship between visual acuity and contrast sensitivity cannot be extrapolated from these graphs. This has been shown through previous work comparing various measures of spatial vision – that is, knowing one measure does not necessarily mean you can predict another measure accurately (Haegerström-Portnoy et al. 2000).

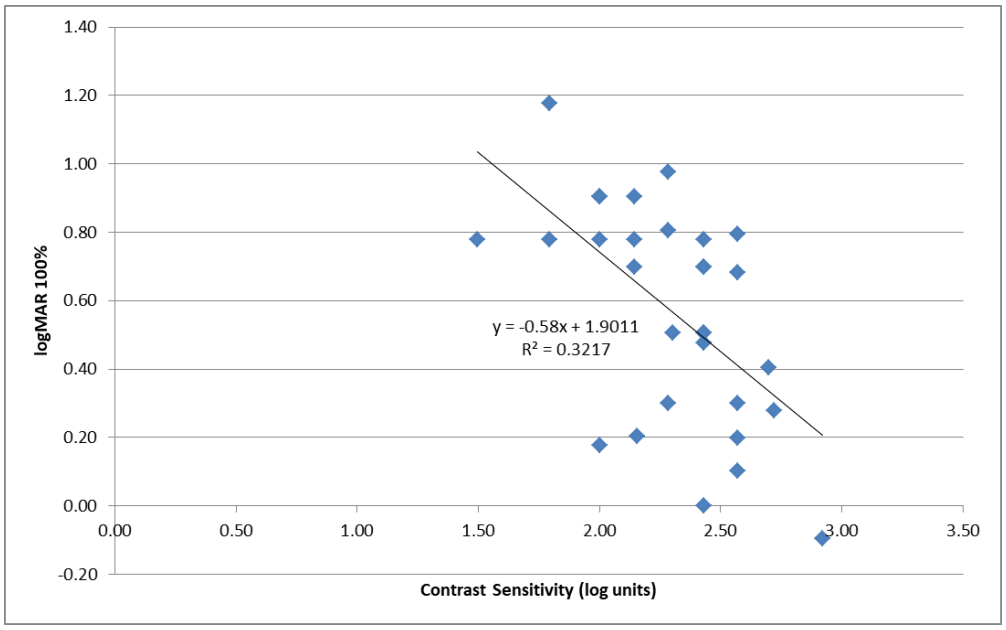

Figure 5.2: Correlation between 100% logMAR visual acuity and contrast sensitivity on the Cambridge Low Contrast Gratings.

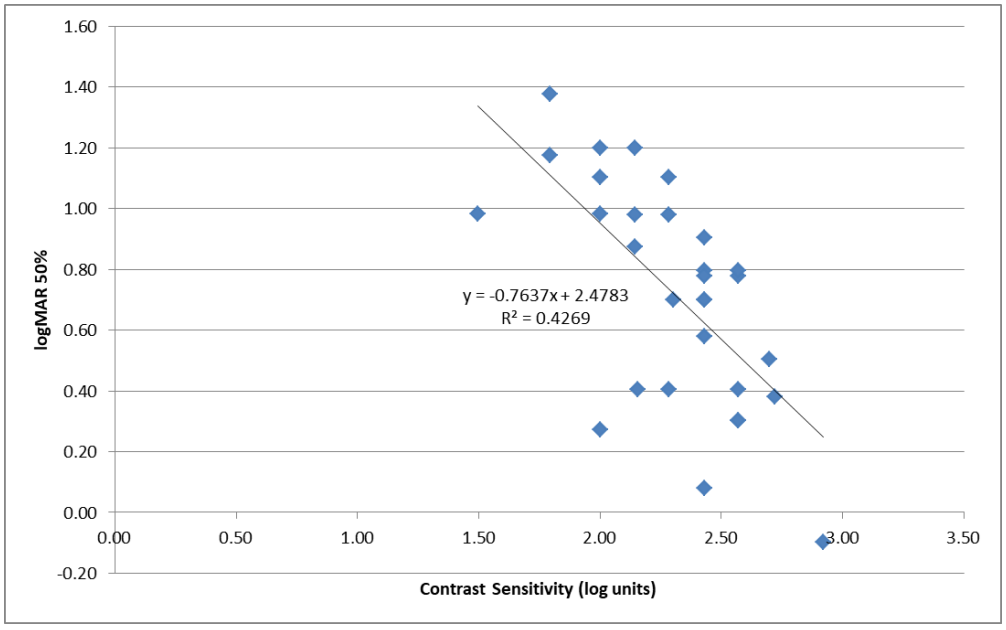

Figure 5.3: Correlation between 50% logMAR visual acuity and contrast sensitivity on the Cambridge Low Contrast Gratings.

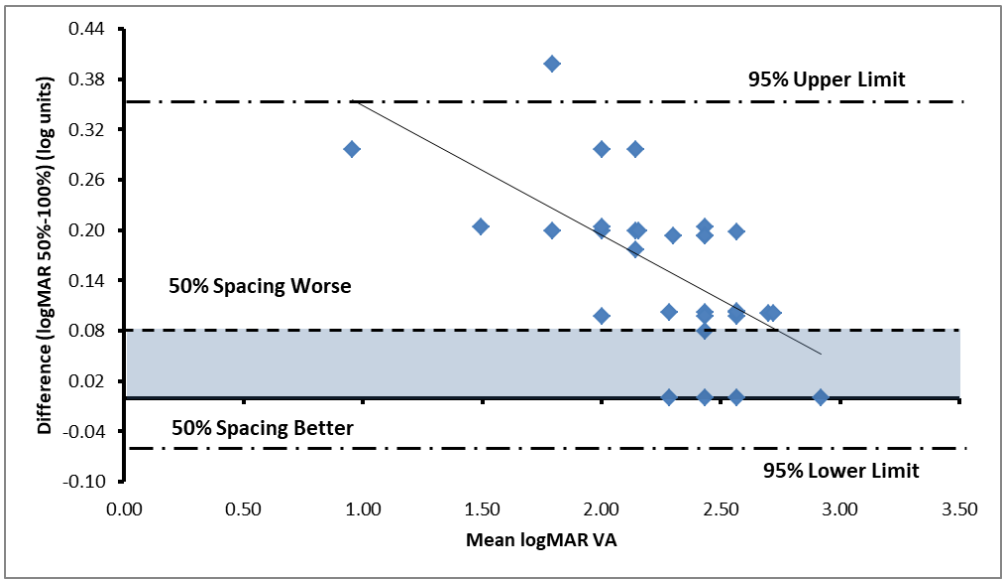

Figure 5.4: Bland-Altman analysis plotting the difference in visual acuity measures versus their mean.

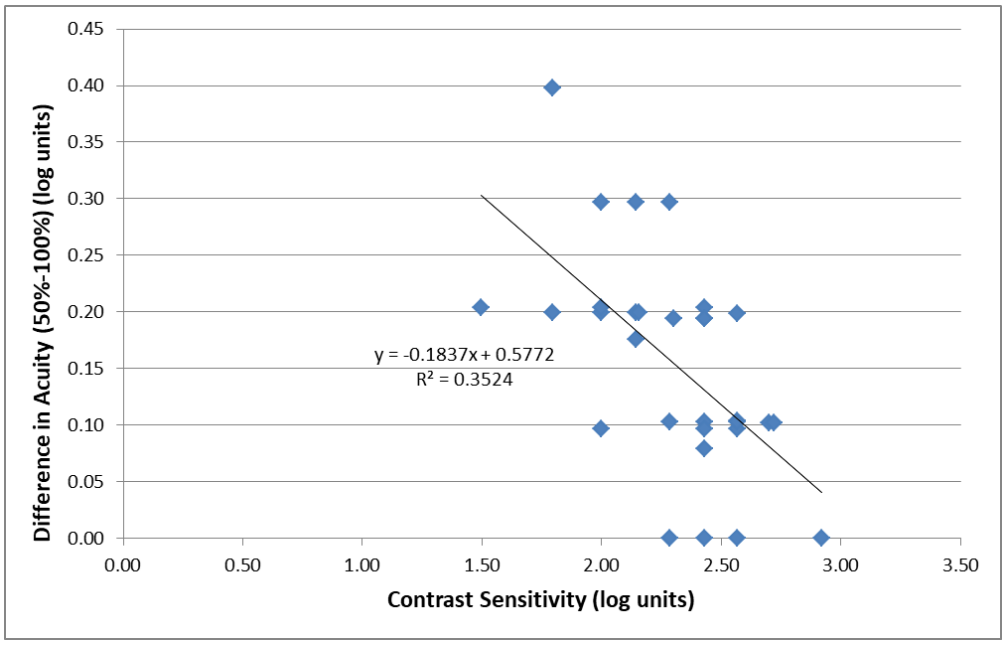

Figure 5.5: Correlation between the difference in visual acuity due to contour interaction compared with contrast sensitivity. Generally, the greater the effect of contour interaction the more reduced the contrast sensitivity.

A Bland-Altman analysis was performed to evaluate the difference in visual acuity measures versus their mean. On average, visual acuity was 0.15 logMAR worse with 50% vs. 100% spacing (equivalent to about a line and a half) (Figure 4.4). This is similar to the finding in the group tested in Chapter 2 (-0.16 logMAR worse with 50% vs. 100%).

The relationship between visual acuity with increased contour interaction was compared to threshold contrast sensitivity (Figure 4.5). A greater difference in visual acuity with 50% compared to 100% Lea symbols (in logMAR) was correlated with decreased contrast sensitivity (in log Michelson contrast sensitivity); with a Pearson correlation coefficient of -0.593 and R^2 value of 0.352 ($p = 3.69 \times 10^{-24}$).

Discussion

In a previous chapter, we attempted to quantify the effect of contour interaction due to flanking bars on visual acuity in children with CVI. The results indicated that the reduction in acuity was greater in the presence of contour bars spaced more closely (50% spacing) as compared to greater spacing (100% spacing). This was found to be consistent with previous work found in the literature which showed a decrease in acuity in the presence of contour interaction in preschool children (Fern et al. 1986; Manny, Fern, and Loshin 1987).

The Cambridge Low Contrast Gratings were designed based on an initial study which utilized grating lines that were difficult to reproduce - therefore, a variation was produced which utilized dot matrix printing and created a test version that was consistent across printings (Della Sala et al. 1985). The original version of the test was not released with age-related norms; in 1988, those norms were measured and published (Wilkins et al. 1988). In the same study, it was determined that the Cambridge Low Contrast Gratings may be most useful in younger populations. In clinical practice, the Cambridge Low Contrast Gratings can be an efficient and simple form of behavioral contrast sensitivity measurement.

Clinicians may find that individuals with visual symptoms have normal Snellen or visual acuity, but a reduction in contrast sensitivity. In children with CVI, the findings can be quite varied. In children with one form of CVI known as periventricular leukomalacia (PVL), children were found to have difficulties with crowding, visual field defects, oculomotor problems, and visual perceptual disturbances, while color vision and contrast sensitivity were found to be well preserved (Jacobson et al. 1996). In general, the children tested in this group had contrast sensitivity values that were quite good. Even though the contrast sensitivity results are quite good, the children still do not have "normal vision." That is, there was no less damage from CVI in this group – ultimately it further emphasizes the point that one cannot predict visual acuity from contrast sensitivity or vice versa, and it further highlights the importance of measuring both for a complete assessment of the child's visual function.

In a more recent study, Good et al. compared visual evoked potential measures of contrast

sensitivity and grating acuity in children with CVI, as well as age-matched normally sighted controls. Their conclusion was that spatial contrast sensitivity and response amplitudes are greatly diminished by CVI (Good, Hou, and Norcia 2012). It is clear that contrast sensitivity remains an important measure of visual function, and may be more reduced in children who are also susceptible to the effects of contour interaction and crowding.

Conclusions

This study compared the relationship between visual acuity, in the presence of contour interaction, and contrast sensitivity in children with CVI. The original premise for this study stemmed from the assumption that even though correlations between spatial vision measures are not always strong, there is still some amount of correlation. Therefore, this investigation examined if those with worse vision function due to increased crowding effects may also expect a reduction in contrast sensitivity. Preliminary findings show a positive correlation between contour interaction and contrast sensitivity - however, the variability is quite large and the ability to predict one from the other is quite low. Teachers and other members of the child's care team may consider utilizing various contrast enhancement techniques to aid in the child's academic and personal success.

For example, even if the child does not have a visual acuity which limits their ability to identify written materials at a certain size level, the child may still benefit from an instrument such as a closed-circuit television magnifier which can allow for contrast enhancement and color reversal. Other possibilities include colored overlays for printed materials, reverse printing of materials (i.e. white print on a black background), digital devices with built in features, and enlargement of print and spacing. From a functionality standpoint, a child with reduced contrast sensitivity should be identified so proper orientation and mobility training may be considered.

In general, consideration of contour interaction and contrast sensitivity may be informative when making recommendations to and determining educational interventions for children with CVI.

References

1. Abramov, I., L. Hainline, J. Turkel, E. Lemerise, H. Smith, J. Gordon, and S. Petry. 1984. Rocket-Ship Psychophysics. Assessing Visual Functioning in Young Children. Investigative Ophthalmology and Visual Science 25 (11): 1307-15.

2. Afshari, MA, NA Afshari, and AB Fulton. 2001. Cortical Visual Impairment in Infants and Children. International Ophthalmology Clinics 41 (1): 159-69.

3. Atkin, A, I Bodis-Wollner, M Wolkstein, A Moss, and S Podos. 1979. Abnormalities of Central Contrast Sensitivity in Glaucoma. American Journal of Ophthalmology 88 (2): 205-11.

4. Atkinson, J, J French, and O Braddick. 1981. Contrast Sensitivity Function of Preschool Children. The British Journal of Ophthalmology 65 (8): 525-29.

5. Banks, Martin S., and Philip Salapatek. 1976. Contrast Sensitivity Function of the Infant Visual System. Vision Research 16 (8).

6. Bansback, N., C. Czoski-Murray, J. Carlton, G. Lewis, L. Hughes, M. Espallargues, C. Brand, and J. Brazier. 2007. Determinants of Health Related Quality of Life and Health State Utility in Patients with Age Related Macular Degeneration: The Association of Contrast Sensitivity and Visual Acuity. Quality of Life Research 16 (3): 533-43.

7. Benedek, György, Krisztina Benedek, Szabolcs Kéri, and Márta Janáky. 2003. The Scotopic Low-Frequency Spatial Contrast Sensitivity Develops in Children between the Ages of 5 and 14 Years. Neuroscience Letters 345 (3): 161-64.

8. Bouma, H. 1970. Interaction Effects in Parafoveal Letter Recognition. Nature 226: 177-78.

9. Bradley, Arthur and Freeman, R.D. 1982. Contrast Sensitivity in Children. Vision Research 22: 953-59.

10. Bradley, A, and R D Freeman. 2018. Contrast Sensitivity in Anisometropic Amblyopia, 467-76.

11. Chung, Susana T.L., and Gordon E. Legge. 2016. Comparing the Shape of Contrast Sensitivity Functions for Normal and Low Vision. Investigative Ophthalmology and Visual Science 57 (1): 198-207.

12. Chung, Susana T.L., Dennis M. Levi, and Gordon E. Legge. 2001. Spatial-Frequency and Contrast Properties of Crowding. Vision Research 41 (14): 1833-50.

13. Coates, Daniel Robert, Jeremy M Chin, and Susana T.L. Chung. 2013. Factors Affecting Crowded Acuity: Eccentricity and Contrast. Optometry Vision Science 90 (7): 996-1005.

14. Cooke, R W I. 2004. Ophthalmic Impairment at 7 Years of Age in Children Born Very Preterm. Archives of Disease in Childhood - Fetal and Neonatal Edition 89 (3): F249-53.

15. Danilova, Marina V, and Valeria M Bondarko. 2007. Foveal Contour Interactions and Crowding Effects at the Resolution Limit of the Visual System. Journal of Vision 7 (2): 25.1–18.

16. Derefeldt, Gunilla, Gunnar Lennerstrand, and Bjorn Lundh. 1979. Age Variations in Normal Human Contrast Sensitivity. Acta Ophthalmologica 57 (4): 679-90.

17. Ellemberg, Dave, Terri L. Lewis, Chang Hong Liu, and Daphne Maurer. 1999. Development of Spatial and Temporal Vision during Childhood. Vision Research 39 (14): 2325-33.

18. Elliott, D B, Bullimore, Patla, and Whitaker. 1996. Effect of a Cataract Simulation on Clinical and Real World Vision. British Journal of Ophthalmology 80 (9): 799-804.

19. Fern, Karen D., Ruth E. Manny, James R. Davis, and Roy R. Gibson. 1986. Contour Interaction in the Preschool Child. American Journal of Optometry Physiological Optics 63 (5): 313-18.

20. Foley, John M. 1994. Human Luminance Pattern-Vision Mechanisms: Masking Experiments Require a New Model. Journal of the Optical Society of America A 11 (6): 1710.

21. Giaschi, Deborah E., David Regan, Stephen P. Kraft, and Angela C. Kothe. 1993. Crowding and Contrast in Amblyopia. Optometry Vision Science 70 (3): 192-97.

22. Good, W. V., C. Hou, and a. M. Norcia. 2012. Spatial Contrast Sensitivity Vision Loss In Children With Cortical Visual Impairment. Investigative Ophthalmology Visual Science, no. Cvi: 7730-34.

23. Good, William V., Chuan Hou, and Anthony M. Norcia. 2012. Spatial Contrast Sensitivity Vision Loss in Children with Cortical Visual Impairment. Investigative Ophthalmology and Visual Science 53 (12): 7730-34.

24. Good, William V., James E. Jan, Susan K. Burden, A. Skoczenski, and T Rowan Candy. 2001. Recent Advances in Cortical Visual Impairment. Developmental Medicine and Child Neurology 43: 56-60.

25. Gwiazda, Jane, Joseph Bauer, Frank Thorn, and Richard Held. 1997. Development of Spatial Contrast Sensitivity from Infancy to Adulthood: Psychophysical Data. Optometry Vision Science 74 (10): 785-89.

26. Haegerström-Portnoy, G, M. Schneck, and J. Brabyn. 1999. Seeing into Old Age: Vision Function beyond Acuity. Optometry and Vision Science 76 (3): 141-58.

27. Haegerström-Portnoy, G, M E Schneck, L a Lott, and J a Brabyn. 2000. The Relation between Visual Acuity and Other Spatial Vision Measures. Optometry and Vision Science: Official Publication of the American Academy of Optometry 77 (12): 653-62.

28. Haegerström-Portnoy, Gunilla, John Brabyn, Marilyn E. Schneck, and Arthur Jampolsky. 1997. The SKILL Card: An Acuity Test of Reduced Luminance and Contrast. Investigative Ophthalmology and Visual Science 38 (1): 207-18.

29. Jacobson, L, U Ek, E Fernell, O Flodmark, and U Broberger. 1996. Visual Impairment in Preterm Children with Periventricular Leukomalacia–Visual, Cognitive and Neuropaediatric Characteristics Related to Cerebral Imaging. Developmental Medicine and Child Neurology 38: 724-35.

30. Jones, Helen S., Merrick J. Moseley, and John R. Thompson. 1994. Reliability of the Cambridge Low Contrast Gratings. Ophthalmic and Physiological Optics 14 (3): 287-89.

31. Khetpal, Vijay, and Sean P. Donahue. 2007. Cortical Visual Impairment: Etiology, Associated Findings, and Prognosis in a Tertiary Care Setting. Journal of American Association for Pediatric Ophthalmology and Strabismus 11 (3): 235-39.

32. Kothe, Angela C., and David Regan. 1990. Crowding Depends on Contrast. Optometry Vision Science 67 (4): 283-86.

33. Leat, Susan J., Naveen K. Yadav, and Elizabeth L. Irving. 2009. Development of Visual Acuity and Contrast Sensitivity in Children. Journal of Optometry 2 (1). Elsevier: 19-26.

34. Leat, Susan J, and Daniela Wegmann. 2004. Clinical Testing of Contrast Sensitivity in Children: Age-Related Norms and Validity. Optometry and Vision Science: Official Publication of the American Academy of Optometry 81 (4): 245-54.

35. Legge, Gordon, and John Foley. 1980. Contrast Masking in Human Vision. Journal of Optical Society of America 70 (12): 1458-71.

36. Levi, Dennis M, Srividhya Hariharan, and Stanley A Klein. 2002. Suppressive and Facilitatory Spatial Interactions in Peripheral Vision: Peripheral Crowding Is Neither Size Invariant nor Simple Contrast Masking. Journal of Vision 2 (2): 3.

37. Manny, Ruth E., Karen D. Fern, and David S. Loshin. 1987. Contour Interaction Function in the Preschool Child. American Journal of Optometry Physiological Optics 64 (9): 686-92.

38. Marron, J A, and I L Bailey. 1982. Visual Factors and Orientation-Mobility Performance. American Journal of Optometry and Physiological Optics 59 (5): 413-26.

39. McKee, Suzanne P., Dennis M. Levi, and J. Anthony Movshon. 2003. The Pattern of Visual Deficits in Amblyopia. Journal of Vision 3 (5): 5.

40. Nielsen, Lisbeth Sandfeld, Sidse Kringelholt Nielsen, Liselotte Skov, and Hanne Jensen. 2007a. Contrast Sensitivity–an Unnoticed Factor of Visual Perception in Children with Developmental Delay: Normal Data of the Cambridge Low Contrast Gratings Test in Children. Journal of Child Neurology 22 (2): 151-55.

41. . 2007b. Contrast Sensitivity - An Unnoticed Factor of Visual Perception in Children with Developmental Delay: Normal Data of the Cambridge Low Contrast Gratings Test in Children. Journal of Child Neurology 22 (2): 151-55.

42. Owsley, C, and M E Sloane. 1987. Contrast Sensitivity, Acuity, and the Perception of Real-World Targets. British Journal of Ophthalmology 71 (10): 791-96.

43. Philip, Swetha Sara, and Gordon N Dutton. 2014. Identifying and Characterising Cerebral Visual Impairment in Children: A Review. Clinical Experimental Optometry: Journal of the Australian Optometrical Association 97 (3): 196-208.

44. Regan, David, and David Neima. 1983. Low-Contrast Letter Charts as a Test of Visual Function. Ophthalmology 90 (10). American Academy of Ophthalmology, Inc: 1192-1200.

45. Rogers, G. L., D. L. Bremer, and L. E. Leguire. 1987. The Contrast Sensitivity Function and Childhood Amblyopia. American Journal of Ophthalmology 104 (1). American Journal Of Ophthalmology: 64-68.

46. Sala, S Della, G Bertoni, L Somazzi, F Stubbe, and A J Wilkins. 1985. Impaired Contrast Sensitivity in Diabetic Patients with and without Retinopathy: A New Technique for Rapid Assessment. Br J Ophthalmology 69 (2): 136-42.

47. Salapatek, P, and MS Banks. 1978. Acuity and Contrast Sensitivity in 1-, 2-, and 3-Month-Old Human Infants. Investigative Ophthalmology and Visual Science 17 (4): 361-65.

48. Scharre, Janice Emigh, Susan A. Cotter, Sandra Stein Block, and Susan A. Kelly. 1990. Normative Contrast Sensitivity Data for Young Children. Optometry and Vision Science 67 (11): 826-32.

49. Simmers, Anita J, Lyle S Gray, Paul V McGraw, and Barry Winn. 1999. Contour Interaction for High and Low Contrast Optotypes in Normal and Amblyopic Observers. Ophthalmic and Physiological Optics. Vol. 19.

50. Slataper, F J. 1950. Age Norms of Refraction and Vision. Arch Ophthal 43: 466-81.

51. Toet, Alexander, and Dennis M. Levi. 1992. The Two-Dimensional Shape of Spatial Interaction Zones in the Parafovea. Vision Research 32 (7): 1349-57.

52. Weymouth, Frank W. 1963. Vision of Children, An Optometric Symposium. Philadelphia: Chilton Books: 119-143.

53. Wilkins, A.J., S Della Sala, L Somazzi, and I Nimmo-Smith. 1988. Age-Related Norms for the Cambridge Low Contrast Gratings, Including Details Concerning Their Design and Use. Clinical Vision Science 2 (3): 201-12.

54. Wolkstein, M, A Atkin, and I Bodis-Wollner. 1980. Contrast Sensitivity in Retinal Disease. Ophthalmology 87 (11). American Academy of Ophthalmology, Inc: 1140-49.

Chapter 6

Contour interaction in CVI and retinal disease

Background

Review of Cerebral Visual Impairment

Cerebral visual impairment (CVI) is the leading cause of vision loss in children in industrialized nations and results from an insult to the developing brain. As described throughout previous chapters, children with CVI have more difficulty with identifying symbols in the presence of nearby contours. The goal of this study was to compare the level to which this difficulty occurs in children with CVI and children with retinal disease without brain damage.

Visual Challenges for Children with CVI

Studies and case reports identify complex visual patterns, arrays, and scenes to be visually challenging for children with CVI. In their study, Dutton et al. identified various behaviors underlying dorsal stream dysfunction that can contribute to an impaired ability to handle complex visual scenes and tasks such as finding a toy in a toy box, finding an item of clothing in a pile of clothing, or seeing a distant object even if it exceeds their resolution limit. This can also create challenges when identifying people in a group, crowded places, and of course, difficulties with reading printed materials (Dutton, McKillop, and Saidkasimova 2006). Common behaviors of children with CVI include a preference for using touch to identify objects, variability in visual field defects, and looking away while reaching (Jan et al. 1987). They also may exhibit light gazing (Jan, Groenveld, and Sykanda 1990), or photophobia (Jan, Groenveld, and Anderson 1993).

Total blindness is rare. In higher-functioning children, functional visual acuity usually tends to be greater than twice the level of visual acuity when tested with Lea symbols or crowded

and uncrowded visual acuity charts with pictures and letters. Generally speaking, children with CVI have normal color vision. Visual field deficit is related to the location of the specific visual pathway damage. Furthermore, contrast sensitivity can be reduced but is not always (Philip and Dutton 2014).

Review of Contour Interaction Effect Observed

In earlier chapters, we evaluated the effect of contour interaction due to flanking bars on visual acuity in children with CVI. As expected, the reduction in acuity was greater in the presence of contour bars spaced more closely (50% spacing) as compared to greater spacing (100% spacing). This is consistent with previous work done by Manny and Fern that showed a decrease in acuity in the presence of contour interaction in preschool children (Fern et al. 1986; Manny, Fern, and Loshin 1987). The expectation is that this effect of contour interaction is greater in children with CVI than in normally sighted children or in children with ocular disease.

Perhaps one of the most extensively studied models of crowding and contour interaction is in individuals with amblyopia. It is well established in the literature that crowding and contour interaction occur in the central visual field of individuals with amblyopia, and this was first reported by Irvine in 1948 (Irvine 1948). More recent work indicates that there is a difference in the effect of crowding in patients with strabismic amblyopia as compared to anisometropic amblyopia (Song, Levi, and Pelli 2014). However, no direct comparison has been made between the effect of contour interaction in children with CVI as compared to children with ocular disease.

Studies on Crowding and Contour Interaction in Visual Impairment

One study evaluated 18 visually impaired patients (varying causes but primarily retinal conditions) using line acuity, single letter acuity, and the Regan repeat-letter test. This data was also compared to 25 age-matched normal controls. They found a significant effect of crowding in 83% of the patients with visual impairment. They also found a significant effect of contour or lateral interactions in 56% of patients with visual impairment (Pardhan 1997).

A systematic review on foveal crowding evaluated three groups and compared these groups to adults with normal vision. The comparison was made to children with normal vision, visually impaired children and adults, and children with CVI. As expected, even normally sighted children show an area of contour interaction 1.5-3x as large as in normally sighted adults. Adults with congenital nystagmus were shown to have larger contour interaction areas and a larger crowding effect as well (about 2x as large as adults with normal vision). This study also found that children with CVI have a magnitude of crowding about 3x the

size of adults with normal vision (Huurneman et al. 2012).

A related concept derives from the useful field of vision (UFoV). Participants with low vision have a tendency to make more errors in the presence of a cluttered field, but this is not due to divided attention (Leat and Lovie-Kitchin 2006).

Study

Purpose

Ocular visual impairment has been extensively studied in many different ways. Children with retinal disease have remained an important sector of vision research. Although retinal disease is better understood, it still remains to be a smaller segment of the population than the growing groups of individuals with cerebral visual impairment (CVI). This study aims to draw further connections between classical forms of visual impairment that are well understood and a segment of visual impairment that remains to be elaborated upon. Children with CVI exhibit a reduction in visual acuity in the presence of increased contour interaction, as compared to normally sighted children. Although the main cause of vision loss may not be well defined in CVI, it is still necessary to compare CVI to ocular forms of visual impairment, such as in the presence of retinal disease. The goal of this study was to examine the contour interaction effect in children with known retinal disease.

Etiology	Number of Subjects
Hydrocephalus	7
Microcephaly	7
Periventricular leukomalacia (white matter damage)	13
Joubert Syndrome	3
Hypoxic Ischemic Encephalopathy/cerebrovascular accident/birth trauma	9
Confirmed diagnosis of CVI, unspecified	3
Infection/drug exposure in utero	3
Injury/malformation of corpus callosum	4
Hemispherectomy	1
Unclear etiology, risk of CVI based on history	12

Table 6.1: Etiologies of CVI subject pool.

Etiology	Number of Subjects
Retinopathy of Prematurity	3
Oculocutaneous/Ocular Albinism	7
Retinitis Pigmentosa	2
Retrolental fibroplasia/PHPV	2
Coloboma	2
Retinoblastoma	2
Achromatopsia	2

Table 6.2: Etiologies of disease subject pool.

Methods

Binocular visual acuity was measured during a comprehensive vision examination for 43 children presenting with a diagnosis of CVI (ages 3-23; mean 9.13 years - etiologies in Table 6.1) and 20 children with confirmed retinal disease (ages 3-29 years; mean 7.6 years - etiologies in Table 6.2).

Single Lea symbols with contour flanker bars at 50%, 100%, and isolated (infinite) spacing were presented in a two-alternative forced choice manner using the apple and the house as the test optotypes. Visual acuity thresholds were determined using the modified acuity card procedure by observation of the child's eye gaze, pointing, and/or naming of the optotype. Isolated symbol measurements were obtained for a subset of the group with retinal disease (13 of the 20 children) and a separate group of 19 children with CVI (ages 4-20 years; mean 9.6 years).

Results

A Bland-Altman analysis is a method that allows one to determine the difference between two measures. A Bland-Altman analysis comparing 100% Lea visual acuity compared to isolated Lea visual acuity was performed for both populations. The difference between the two measures was found to be -0.07 logMAR (less than one line) for children with CVI and -0.08 logMAR for children with retinal disease (less than one line).

A similar analysis was performed to compare 100% Lea visual acuity versus 50% Lea visual acuity for both populations. For children with CVI, the difference was found to be -0.15 logMAR (50% was about 1.5 lines worse than 100%). For the children with retinal disease, the difference was identical at -0.15 logMAR (50% was about 1.5 lines worse as well).

The final comparison was made between isolated Lea symbols and 50% Lea visual acuity for

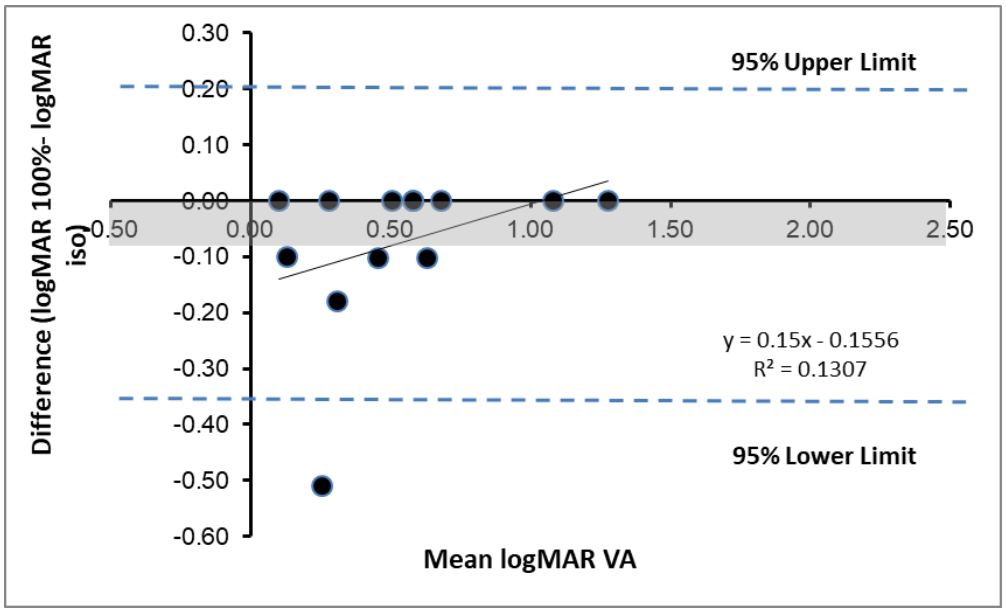

Figure 6.1: Bland-Altman comparison of logMAR 100% and logMAR isolated visual acuity for children with retinal disease.

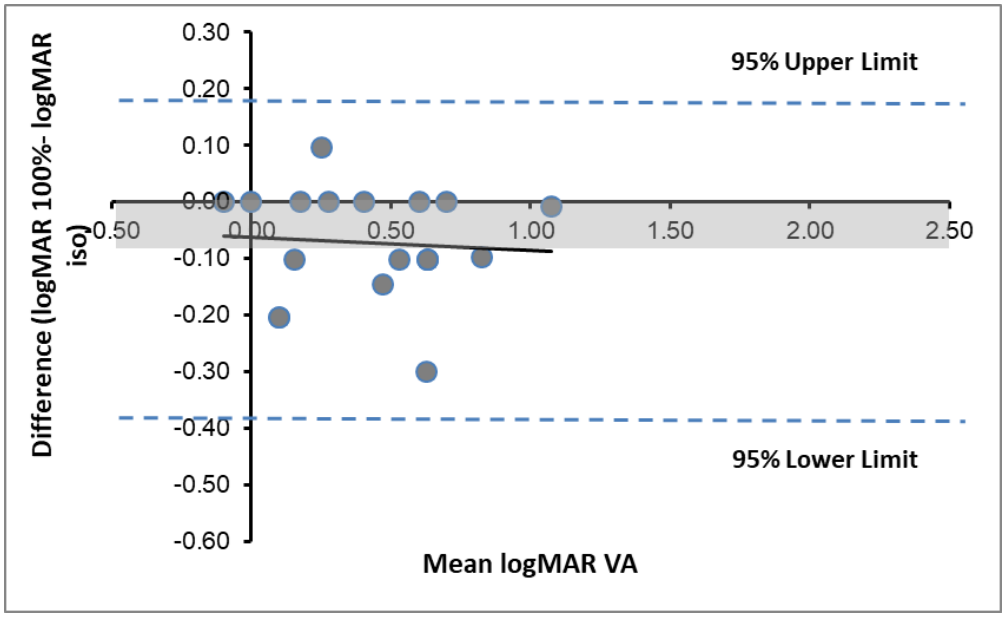

Figure 6.2: Bland-Altman analysis of logMAR 100% versus logMAR isolated for children with CVI.

both groups. The group with CVI showed the largest difference of all comparisons at -0.22 logMAR (about 2 lines worse with 50% as compared to isolated symbols). For the group

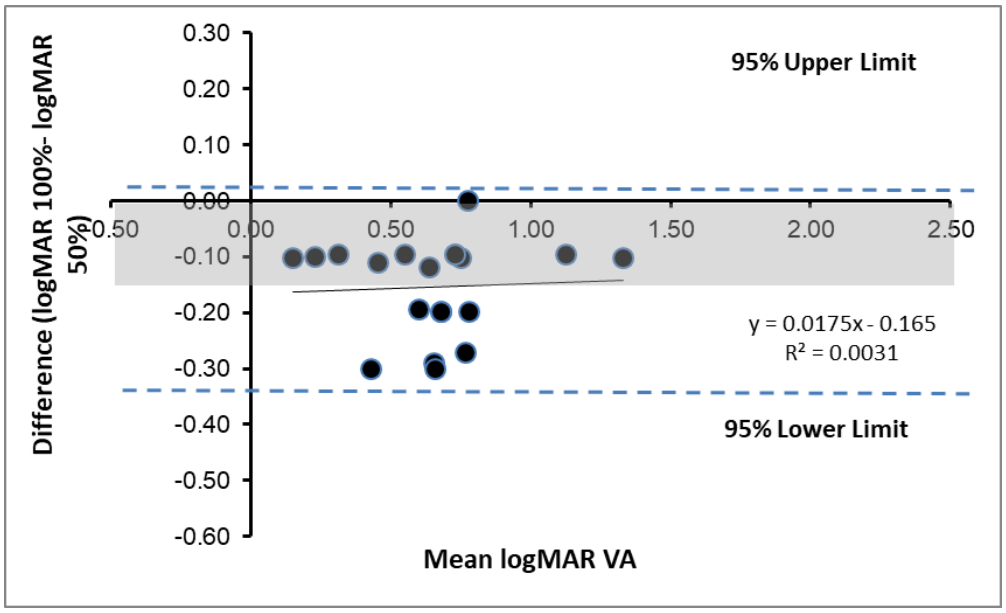

Figure 6.3: Bland-Altman comparison of logMAR 100% and logMAR 50% visual acuity for children with retinal disease.

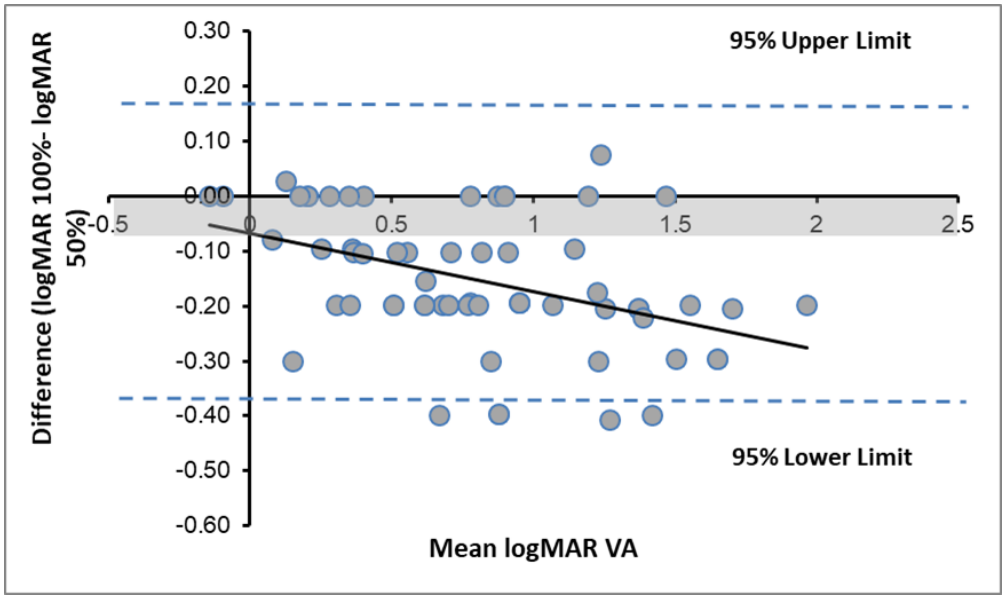

Figure 6.4: Bland-Altman analysis of logMAR 100% versus logMAR 50% for children with CVI.

with retinal disease, the difference between measures was -0.19 logMAR (also about 2 lines worse with 50% as compared to isolated symbols).

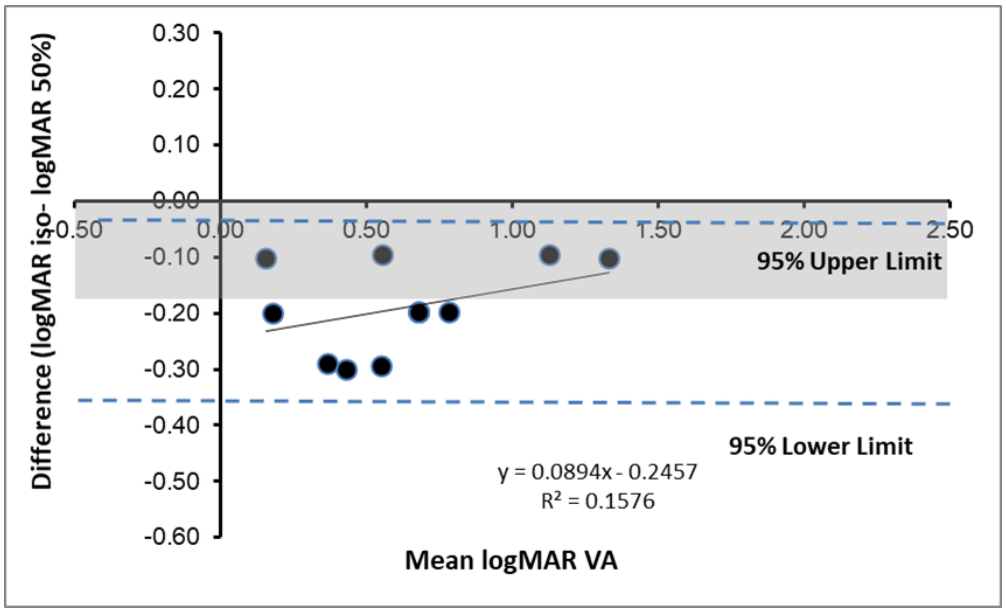

Figure 6.5: Bland-Altman comparison of logMAR isolated and logMAR 50% visual acuity for children with retinal disease.

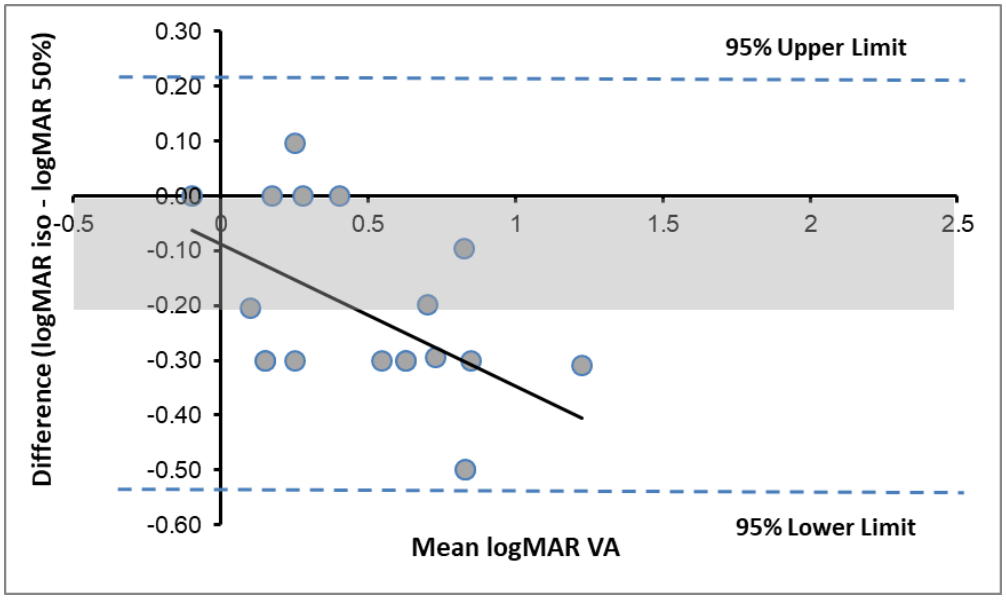

Figure 6.6: Bland-Altman analysis of logMAR isolated versus logMAR 50% for children with CVI.

Example Case Discussion

Case Report 1

P.A. is a 7 year old female who presents for a comprehensive vision exam as a new patient to the Special Visual Assessment Clinic (SVAC). P.A.'s history is significant for oculocutaneous albinism. She is in good health. Her best spectacle correction is +4.50 -1.50 x 160 and +3.50 -3.50 x 020. She has horizontal nystagmus which is worse in extreme gaze. Her logMAR visual acuities for 100%, and 50% spacing are 0.70 logMAR, and 0.80 logMAR, respectively. Her Cambridge Contrast sensitivity was measured to be 0.52% (measured in Michelson contrast). Her color vision and visual fields are normal. P.A. is a rather typical patient with OCA. P.A. is affected by contour interaction, demonstrating a line difference between 100% and 50%.

Case Report 2

G.V. is an 11 year old female who presents for a comprehensive vision exam as a new patient to the Special Visual Assessment Clinic (SVAC). G.V.'s history is significant for retinitis pigmentosa. She is in good health. Her best spectacle correction is +4.50 -3.00 x 005 and +4.50 -3.00 x 175. Her ocular health is significant for signs of retinitis pigmentosa, including optic nerve pallor and scattered RPE clumping. Her logMAR visual acuities for isolated, 100%, and 50% spacing are 0.58 logMAR, 0.68 logMAR, and 0.78 logMAR, respectively. Her Cambridge Contrast sensitivity was severely reduced to 2.70% (measured in Michelson contrast). Her color vision was normal and she has restricted visual fields.

G.V. is an excellent example of a different type of retinal condition that can be quite debilitating with respect to all areas of visual function. Not surprisingly, G.V. demonstrates a much greater reduction in visual acuity in the presence of increased contour interaction as compared to a patient with OCA such as P.A.

From these two case reports, it is clear that the nature of retinal disease is a particularly important factor when determining the susceptibility to reductions in visual acuity in the presence of crowding and contour interaction. The comparison to CVI is quite variable depending on the cause of the retinal disease, and averaging this data does not highlight the differences due to etiology of retinal disease.

Discussion

This study compared the effect of varying levels of contour interaction on visual acuity in children with CVI and children with retinal disease. When comparing 100% and isolated spacing symbols, 100% and 50% spacing symbols, and 50% and isolated spacing symbols there was no significant difference between the group with CVI and the group with retinal disease.

However, looking at the data more closely, it is clear that there is a trend for increasingly worse acuity with increased contour interaction in all comparisons for the CVI group. Comparatively, this is not the case for the group with disease, as the Bland-Altman slope shows a relatively flat line across all visual acuity levels in all comparisons made. This would indicate that the two groups behave quite differently in the presence of contour interaction, despite the nearly identical averages. The prediction is that a child with retinal disease would not be subject to as much contour interaction as compared to a child with CVI, and the slope of the trend still supports this idea.

If the same pattern would appear with an even larger sample size, it may be reasonable to infer that visual impairment in general will cause difficulties with contour interaction and crowding as shown in other studies as well. However, it is likely that the mechanism by which this difficulty occurs is different for children with CVI versus children with retinal disease. Lateral interactions at the retinal level may play a larger role in patients who have damage to the retinal integrity. Cortical processing and other higher level processing may be the more appropriate explanation for children with CVI.

As discussed in the case comparison above, cause of retinal disease is particularly important when determining the likelihood that contour interaction and crowding may affect visual performance. Children with conditions such as oculocutaneous albinism (OCA) typically have the same number of nerve fibers, however, they exhibit a loss of the foveal contour (foveal hypoplasia). On the other hand, a child with retinitis pigmentosa (RP) would exhibit increasing levels of loss of retinal sensitivity as the progressive condition begins affecting more and more parts of the peripheral and central retina. Furthermore, conditions such as OCA will not typically affect contrast sensitivity levels or visual field performance, whereas both can be profoundly affected in children with RP. As always, it is important to evaluate each child as an individual and attempt to accurately assess that specific child's visual challenges.

Conclusions

Special care must be given when drawing conclusions about the effect of contour interaction in the presence of retinal disease. The cause of visual impairment is particularly important when determining the likelihood of and degree of reduction in visual acuity due to contour interaction and ultimately crowding. Children with visual impairment, independent of the cause, should be evaluated by a low vision optometrist who is able to advocate for the student to receive the appropriate services for vision services as he or she advances throughout the education system.

References

1. Dutton, G N, E C A McKillop, and S Saidkasimova. 2006. Visual Problems as a Result of Brain Damage in Children. The British Journal of Ophthalmology 90 (8): 932-33.

2. Fern, Karen D., Ruth E. Manny, James R. Davis, and Roy R. Gibson. 1986. Contour Interaction in the Preschool Child. American Journal of Optometry & Physiological Optics 63 (5): 313-18.

3. Huurneman, Bianca, F Nienke Boonstra, Ralf Fa Cox, Antonius Hc Cillessen, and Ger Van Rens. 2012. A Systematic Review on Foveal Crowding in Visually Impaired Children and Perceptual Learning as a Method to Reduce Crowding. BMC Ophthalmology 12 (1). 27.

4. Irvine, SR. 1948. Amblyopia Ex Anopsia. Observations on Retinal Inhibition, Scotoma, Projection, Light Difference Discrimination and Visual Acuity. Transactions of the American Ophthalmological Society 46: 527-75.

5. Jan, J E, M Groenveld, and D P Anderson. 1993. Photophobia and Cortical Visual Impairment. Developmental Medicine and Child Neurology 35 (6): 473-77.

6. Jan, J E, M Groenveld, and A M Sykanda. 1990. Light-Gazing by Visually Impaired Children. Dev Med Child Neurol 32 (9): 755-59.

7. Jan, J E, M Groenveld, A M Sykanda, and C S Hoyt. 1987. Behavioural Characteristics of Children with Permanent Cortical Visual Impairment. Developmental Medicine and Child Neurology 29 (5): 571-76.

8. Leat, Susan J., and Jan Lovie-Kitchin. 2006. Visual Impairment and the Useful Field of Vision. Ophthalmic and Physiological Optics 26 (4): 392-403.

9. Manny, Ruth E., Karen D. Fern, and David S. Loshin. 1987. Contour Interaction Function in the Preschool Child. American Journal of Optometry Physiological Optics 64 (9): 686-92.

10. Pardhan, Shahina. 1997. Crowding in Visually Impaired Patients: Contour Interaction and/or Gaze- Selection Defects? Neuro-Ophthalmology 18 (2): 59-65.

11. Philip, Swetha Sara, and Gordon N Dutton. 2014. Identifying and Characterising Cerebral Visual Impairment in Children: A Review. Clinical Experimental Optometry: Journal of the Australian Optometrical Association 97 (3): 196-208.

12. Song, Shuang, DM Levi, and DG Pelli. 2014. A Double Dissociation of the Acuity and Crowding Limits to Letter Identification, and the Promise of Improved Visual Screening. Journal of Vision 14: 1-37.

Chapter 7

Appendix

Chapter 2 CVI Raw Data

ID	Gender	Birthdate	Age at exam	logMAR 100%	logMAR 50%	Diagnosis
AgSa1617	M	4/8/2014	3	0.28	0.48	spina bifida, terminal myelocystocele
AsEm111014	F	12/18/2004	9	0.81	1.10	CP, delayed myelination, autism
AtJa51812	M	10/5/1991	20	0.51	0.70	Grade 3 leukomalacia, spastic quadriplegia, slight asthma, CVI
BaDe121015	F	1/24/2011	4	0.90	1.20	Joubert syndrome (developmental delay and cerebellar vermis agenesis/hypoplasia)
BaSh102014	M	11/2/2004	9	-0.10	-0.10	CP, in utero stroke
BeSo103014	F	9/30/2000	13	0.23	0.23	hypotonia, developmental delay, chromosal abnormality of 17 and 10
BeVi112414	F	12/9/2009	4	0.78	0.98	CP, strab, CVI
CoEb92914	F	4/27/2005	9	0.30	0.40	microcephaly
CoMa103014	M	1/19/2006	8	0.20	0.40	small ventricles, corpus callosum
CoOl52214	M	7/7/2003	10	0.98	0.98	microcephaly, underdevelopment of frontal lobes, dysplastic retinas
CuJi41417	F	1/23/2012	4	0.38	0.58	neonatal infection, CVI, delayed visual maturation
DeAi4915	M	9/4/2004	10	0.78	0.98	ROP, CVI/PVL
DeAl41017	F	1/8/2010	7	0.68	1.08	developmental delay, microcephaly
DeHe6216	F	11/2/2006	9	0.20	0.20	gross motor delays, S&L disorder, ET
DeSa62217	F	12/7/2006	10	0.68	0.88	microcephaly
DoAn111615	F	10/2/2003	12	0.40	0.51	microcephaly, hypertelorism
EsYa111917	F	10/3/2001	16	0.20	0.40	CP, schizencephaly, seizure, developmental delay
GoAa52214	M	5/13/2009	4	0.48	0.58	optic neuropathy, arachnoid cyst, hydrocephalus, CNS/VP shunt
GoFo83115	M	4/19/2009	6	0.57	0.98	low muscle tone, developmental delay
GrLe3416	M	3/23/2011	5	0.10	0.07	PVL
GrRo91117	M	3/2/2013	4	0.58	0.78	seizures/ischemic brain injuries/mini strokes/CP/ developmental delay/CVI
GrSi10914	F	9/11/2009	5	0.00	0.08	CP, hx of middle cerebral artery CVA

ID	Gender	Birthdate	Age at exam	logMAR 100%	logMAR 50%	Diagnosis
HeEr12715	M	11/28/2012	3	0.90	1.10	congenital disorder of glycosylation, cerebellar hypoplasia/atrophy
HiMi31716	M	8/15/2002	13	0.78	0.98	premature, mild case of ROP, hydrocephalus
HoBr111615	M	6/25/1999	16	0.18	0.27	CP, developmental delay, CVI
KaAr32917	M	5/15/2009	8	0.58	0.78	CP and birth asphyxia
LeVi71017	M	5/13/2008	9	0.28	0.48	CP, autism, seizure disorder
LoJo92712	M	9/12/2001	11	0.78	1.18	premature, drug exposure in utero, shaken baby syndrome, optic nerve atrophy, CVI, seizure disorder
LoRu6616	M	11/9/1995	20	0.18	0.58	TBI from car accident, CP, seizures
MaJa32317	M	5/6/2011	6	0.70	1.00	minor dysmorphic corpus callosum
MaUr8116	M	9/12/2010	6	0.60	0.60	PVL, high myopia
McMa6616	M	3/18/2005	11	0.18	0.28	hydrocephalus, microgyria, chiari malformation
McVi91715	F	4/16/2004	11	0.68	0.78	chromosomal disorder, CP
MiMa7714	F	3/4/2008	6	0.54	0.64	CP, CVI
MoCa81116	F	1/1/1996	20	0.60	0.80	CP, dev delay, ROP, RD, Cataracts
MuEd72017	M	6/4/2008	9	0.28	0.28	possible CVI
NeAk112217	M	12/16/2007	9	1.00	1.20	CVI due to shaken baby syndrome
OwKa11713	F	1/28/2008	5	0.70	0.90	ROP, CP, developmental delays
PaAl121715	F	11/25/2008	7	0.70	0.80	PVL, ONA
PaAn61616	F	8/31/1987	23	0.68	1.08	CP and CVI
PoEl91715	F	9/30/2004	10	0.28	0.38	thin/absent myelination around corpus callosum and developmental delay
PrAn12317	F	11/3/2006	10	0.54	0.70	CP, CVI
RaAy42116	F	7/26/1999	16	0.90	1.20	hydrocephalus, CP, seizure disorder, CVI
RoEt72017	M	9/14/2011	6	0.18	0.18	PVL

ID	Gender	Birthdate	Age at exam	logMAR 100%	logMAR 50%	Diagnosis
RoOc112213	M	10/8/2008	5	0.51	0.70	drug exposure in utero
RoSu101413	F	10/8/2008	5	0.51	0.70	infantile nystagmus
SaCh5412	F	10/11/2006	4	0.10	0.30	mild CP, PVL
SaJo52412	M	5/10/2004	8	0.78	0.78	developmental delay, strabismus, nystagmus
SoLe32912	F	6/14/1998	13	0.20	0.30	neonatal meningitis, secondary hydrocephalus, CVI
TaSh62317	F	5/23/2002	15	0.88	0.88	TBI
TeDa91516	M	11/27/2005	10	0.20	0.30	left hemispherectomy, right hemianopsia
ThAs92214	M	5/24/2008	6	0.30	0.40	Joubert's syndrome, pre-fragile X count 59
ThBl111714	M	2/15/1996	18	1.18	1.38	microcephaly, CP, hypotonia
ThJo1716	M	5/10/2004	11	0.80	0.80	Developmental delay, nystagmus
ViBr632016	M	11/10/2010	5	0.40	0.60	in utero stroke ONH vs. missing optic nerve tract
WeOz12101 5	M	11/11/2011	4	0.78	1.00	microcephaly
WhHa82216	M	9/2/2006	9	0.40	0.40	premature, high myope
WiSk12516	F	2/12/2006	9	0.70	0.88	CVI
WuMa10261 5	M	4/8/2012	3	0.58	0.78	hypoxic ischemic encephalopathy in utero, occipital cortex injury, likely CVI
MoEd112917	M	3/28/2010	7	0.40	0.6	Joubert syndrome

Chapter 2 Normal Raw Data

ID	Gender	Birthdate	Age at exam	logMAR 100%	logMAR 50%
Alle72817	F	9/11/2007	9	-0.10	-0.10
BaRa61516	F	7/10/2013	3	0.10	0.30
BiAu61716	M	10/23/2006	9	-0.09	0.00
BoZe1617	M	12/6/2013	3	0.10	0.20
BrPr1417	M	8/27/2011	5	0.10	0.20
BuAn63017	F	7/6/2012	4	0.00	0.10
ChAl71516	M	5/21/2009	7	0.00	0.00
ChLo82416	M	7/1/2008	8	-0.10	-0.10
ChMy52716	F	11/28/2011	4	0.00	0.00
ChOl7517	M	7/23/2006	10	-0.10	-0.10
ChWi21017	M	8/5/2008	8	0.10	0.20
CoDa11117	F	6/2/2012	4	0.00	0.00
CoJa3117	M	8/12/2009	7	0.00	0.00
CoMi11117	M	8/24/2009	7	-0.10	-0.10
DaJa51816	M	5/9/2011	5	0.00	0.00
DhAk72817	M	10/31/2007	9	-0.10	0.00
DoDa52516	M	7/3/2011	4	0.00	0.10
DuVi7517	F	12/15/2010	6	-0.10	0.00
FiCh52716	F	8/4/2011	4	0.00	0.10
FrLi6116	F	7/6/2008	7	0.00	0.00
GaAl7717	F	7/27/2012	5	0.10	0.10
HaAu2817	F	3/23/2008	8	-0.10	0.00

ID	Gender	Birthdate	Age at exam	logMAR 100%	logMAR 50%
HaEz1317	M	11/28/2013	3	0.00	0.10
JuAd52016	F	5/13/2008	8	0.00	0.10
LiSu10617	F	unknown	9	-0.10	0.00
LiMa41317	F	10/19/2005	11	-0.10	-0.10
LuKa12017	F	1/31/2011	5	0.00	0.00
LuMa92717	F	3/28/2014	4	0.00	0.10
MaAi7717	M	12/8/2009	7	-0.10	-0.10
MeAv11317	F	5/16/2008	8	-0.10	0.00
RaGa41417	M	10/19/2013	3	0.00	0.00
RaRe71417	M	6/29/2009	8	-0.10	-0.10
ReGi22417	F	12/31/2010	6	0.00	0.10
RiNa2817	M	8/4/2011	5	0.00	0.00
RoCa31017	F	11/12/2007	9	0.20	0.20
SaCo83017	F	6/15/2012	5	0.00	0.10
SzEm9117	F	9/18/2012	4	0.00	0.10
TaAn3817	F	2/25/2011	6	0.20	0.30
UnSo3817	F	7/5/2011	5	0.00	0.00
ViLa62117	F	6/2/2012	5	0.00	0.00
WiDa62817	F	10/31/2012	4	0.00	0.00
WiMi62817	F	1/18/2011	6	-0.10	-0.10
ZhJa9117	M	8/10/2012	5	0.10	0.00

Chapter 3 CVI Raw Data

ID	Gender	Birthdate	Age at exam	Diagnosis	logMAR 100%	logMAR 50%	logMAR iso
BeVi41317	F	12/9/2009	7	CP, strab, CVI	0.68	1.08	0.58
DeAl41017	F	1/8/2010	7	developmental delay, microcephaly	0.68	1.08	0.58
DeHe6216	F	11/2/2006	9	gross motor delays, S&L disorder, ET	0.20	0.20	0.00
DeSa62217	F	12/7/2006	10	microcephaly	0.68	0.88	0.58
GrLe61716	M	3/23/2011	5	alternating exotropia, PVL	0.00	0.30	0.00
KaAr32917	M	5/15/2009	8	CP and birth asphyxia	0.58	0.78	0.48
LoJo5216	M	9/12/2001	14	premature, drug exposure in utero, shaken baby syndrome, optic atrophy and CVI	1.08	1.38	1.07
MaJa32317	M	5/6/2011	6	minor dysmorphic corpus callosum	0.70	1.00	0.70
McVi91715	F	4/16/2004	13	chromosomal disorder, CP	0.78	0.78	0.48
MiMa71116	F	3/4/2008	8	CP, CVI, VP shunt for hydrocephalus	0.20	0.40	0.10
MoCa81116	F	1/1/1996	20	CP, dev delay, ROP, RD, Cataracts	0.60	0.80	0.60
MuEd72017	M	6/4/2008	9	CVI risk	0.28	0.28	0.28
PrAn12317	F	11/3/2006	10	CP, developmental delay, CVI	0.54	0.70	0.40
RoEt72017	M	9/14/2011	6	PVL	0.18	0.18	0.18
Scls81216	F	1/20/2007	9	seizures	-0.10	-0.10	-0.10
TaSh62317	F	5/23/2002	15	TBI	0.88	0.88	0.78
TeDa91516	M	11/27/2005	10	left hemispherectomy, right hemianopsia	0.20	0.30	0.00
ThAs112816	M	5/24/2008	8	Joubert's syndrome, pre fragile X count 59	0.20	0.20	0.30
WhHa82216	M	9/2/2006	9	premature, high myope	0.40	0.40	0.40

Chapter 3 Normal Raw Data

ID	Gender	Birthdate	Age at exam	logMAR 100%	logMAR 50%	logMAR iso
Alle72817	F	9/11/2007	9	-0.10	-0.10	-0.10
BaRa61516	F	7/10/2013	3	0.20	0.00	0.00
BiAu61716	M	10/23/2006	9	-0.09	0.00	-0.09
BoZe1617	M	12/6/2013	3	0.10	0.20	0.10
BrPr1417	M	8/27/2011	5	0.10	0.20	0.00
BuAn63017	F	7/6/2012	4	0.00	0.10	0.00
ChAl71516	F	5/21/2009	7	0.00	0.00	0.00
ChLo82416	M	7/1/2008	8	-0.10	-0.10	-0.10
ChOl7517	M	7/23/2006	10	-0.10	-0.10	-0.10
ChWi21017	M	8/5/2008	8	0.10	0.20	0.10
CoDa11117	F	6/2/2012	4	0.00	0.00	-0.10
CoJa3117	M	8/12/2009	7	0.00	0.00	0.00
CoMi11117	M	8/24/2009	7	-0.10	-0.10	-0.10
DhAk72817	M	10/31/2007	9	-0.10	0.00	-0.10
DuVi7517	F	12/15/2010	6	-0.10	0.00	-0.10
GaAl7717	F	7/27/2012	5	0.10	0.10	0.10
HaAu2817	F	3/23/2008	8	-0.10	0.00	-0.10
HaEz1317	M	11/28/2013	3	0.00	0.10	0.00
LiMa41317	F	10/19/2005	11	-0.10	-0.10	-0.10
LuKa12017	F	1/31/2011	5	0.00	0.00	-0.10
MaAi7717	M	12/8/2009	7	-0.10	-0.10	-0.10
MeAv11317	F	5/16/2008	8	-0.10	0.00	-0.10
RaGa41417	M	10/19/2013	3	0.00	0.00	0.00
RaRe71417	M	6/29/2009	8	-0.10	-0.10	-0.10
ReGi22417	F	12/31/2010	6	0.00	0.10	0.00
RiNa2817	M	8/4/2011	5	0.00	0.00	-0.10
RoCa31017	F	11/12/2007	9	0.20	0.20	0.20
TaAn3817	F	2/25/2011	6	0.20	0.30	0.20
UnSo3817	F	7/5/2011	5	0.00	0.00	0.00
ViLa62117	F	6/2/2012	5	0.00	0.00	0.00
WiDa62817	F	10/31/2012	4	0.00	0.00	0.00
WiMi62817	F	1/18/2011	6	-0.10	-0.10	-0.10

Chapter 4 CVI Raw Data

ID	Gender	Birthdate	Age at exam	Diagnosis	Cardiff VA logMAR	logMAR 100%	logMAR 50%
AsEm111014	F	12/18/2004	9	CP, delayed myelination, autism	0.30	0.81	1.10
BaDe121015	F	1/24/2011	4	Joubert syndrome (developmental delay and cerebellar vermis agenesis/hypoplasia)	0.57	0.90	1.20
BeSo103014	F	9/30/2000	13	hypotonia, developmental delay, chromosal abnormality of 17 and 10	0.00	0.23	0.23
BeVi112414	F	12/9/2009	6	CP, strab, CVI	0.40	0.70	0.88
CoMa103014	M	1/19/2006	8	small ventricles, corpus callosum	0.00	0.20	0.40
DeAi4915	M	9/4/2004	10	ROP, CVI/PVL	0.50	0.78	0.98
GrLe61716	M	3/23/2011	5	alternating exotropia, PVL	0.00	0.00	0.30
HeEr12715	M	11/28/2012	3	congenital disorder of glycosylation, cerebellar hypoplasia/atrophy	0.30	0.90	1.10
LoJo5216	M	9/12/2001	14	premature, drug exposure in utero, shaken baby syndrome, optic atrophy and CVI	0.63	1.08	1.38
MaUr8116	M	9/12/2010	6	PVL, high myopia	0.10	0.60	0.60
MoEd61215	M	3/28/2010	5	Joubert syndrome, oculomotor apraxia	0.60	1.10	1.10
RaAy42116	F	7/26/1999	16	hydrocephalus, CP, seizure disorder, CVI	0.60	0.90	1.20
ThBl111714	M	2/15/1996	18	microcephaly, CP, hypotoni	0.60	1.18	1.38
WiSk12516	F	2/12/2006	9	CVI	0.50	0.70	0.88
WuMa102615	M	4/8/2012	3	hypoxic ischemic encephalopathy in utero, occipital cortex injury, likely CVI	0.30	0.58	0.78

Chapter 5 CVI Raw Data

ID	Gender	Birthdate	Age at exam	Diagnosis	logMAR 100%	logMAR 50%	Cambridge
AsEm111014	F	12/18/2004	9	CP, delayed myelination, autism	0.81	1.10	0.52%
AtJa51812	M	10/5/1991	20	Grade 3 leukomalacia, spastic quadriplegia, slight asthma, CVI	0.51	0.70	0.50%
BaDe121015	F	1/24/2011	4	Joubert syndrome (developmental delay and cerebellar vermis	0.90	1.20	0.72%
BaSh102014	M	11/2/2004	9	CP, in utero stroke	-0.10	-0.10	0.12%
BeVi112414	F	12/9/2009	4	CP, strab, CVI	0.78	0.98	0.72%
CoEb92914	F	4/27/2005	9	microcephaly	0.30	0.40	0.52%
CoMa103014	M	1/19/2006	8	small ventricles, corpus callosum	0.20	0.40	0.70%
CoOl52214	M	7/7/2003	10	underdevelopment of frontal lobes, dysplastic retinas	0.98	0.98	0.52%
DeAi4915	M	9/4/2004	10	ROP, CVI/PVL	0.78	0.98	3.20%
DoAn111615	F	10/2/2003	12	microcephaly, hypertelorism	0.40	0.51	0.20%
GoAa52214	M	5/13/2009	4	optic neuropathy, arachnoid cyst, hydrocephalus, CNS/VP shunt	0.48	0.58	0.37%
GrSi10914	F	9/11/2009	5	CP, hx of middle cerebral artery CVA	0.00	0.08	0.37%
HeEr12715	M	11/28/2012	3	congenital disorder of glycosylation, cerebellar hypoplasia/atrophy	0.90	1.10	1%
HiMi31716	M	8/15/2002	13	premature, mild case of ROP, hydrocephalus	0.78	0.98	1%
HoBr111615	M	6/25/1999	16	CP, developmental delay, CVI	0.18	0.27	0.27%
LoJo92712	M	9/12/2001	11	premature, drug exposure in utero, shaken baby syndrome, optic nerve atrophy, CVI, seizure disorder	0.78	1.18	1.60%
McVi91715	F	4/16/2004	11	chromosomal disorder, CP	0.68	0.78	0.27%
OwKa11713	F	1/28/2008	5	ROP, CP, developmental delays	0.70	0.90	0.37%
PaAl121715	F	11/25/2008	7	PVL, ONA	0.70	0.80	0.37%
PoEl91715	F	9/30/2004	10	thin/absent myelination around corpus callosum and developmental delay	0.28	0.38	0.19%
RaAy42116	F	7/26/1999	16	hydrocephalus, CP, seizure disorder, CVI	0.90	1.20	1%
RoOc112213	M	10/8/2008	5	drug exposure in utero	0.51	0.70	0.37%
RoSu101413	F	10/8/2008	5	infantile nystagmus	0.51	0.70	0.37%
SaCh5412	F	10/11/2006	4	mild CP, PVL	0.10	0.30	0.27%
SaJo52412	M	5/10/2004	8	developmental delay, strabismus, nystagmus	0.78	0.78	0.37%
SoLe32912	F	6/14/1998	13	neonatal meningitis, secondary hydrocephalus, CVI	0.20	0.30	0.27%
ThAs92214	M	5/24/2008	6	Joubert's syndrome, pre-fragile X count 59	0.30	0.40	0.27%
ThBl111714	M	2/15/1996	18	microcephaly, CP, hypotonia	1.18	1.38	1.60%
ThJo1716	M	5/10/2004	11	Developmental delay, nystagmus	0.80	0.80	0.27%
WiSk12516	F	2/12/2006	9	CVI	0.70	0.88	0.72%

Chapter 5 Normal Raw Data

ID	Gender	Birthdate	Age at exam	logMAR 100%	logMAR 50%	Cambridge
Alle72817	F	9/11/2007	9	-0.10	-0.10	0.14%
BuAn63017	F	7/6/2012	4	0.00	0.10	0.27%
ChOl7517	M	7/23/2006	10	-0.10	-0.10	0.14%
DhAk72817	M	10/31/2007	9	-0.10	0.00	0.14%
DuVi7517	F	12/15/2010	6	-0.10	0.00	0.14%
GaAl7717	F	7/27/2012	5	0.10	0.10	0.19%
LiSu10617	F	unknown	9	-0.10	0.00	0.14%
LuMa92717	F	3/28/2014	4	0.00	0.10	0.14%
MaAi7717	M	12/8/2009	7	-0.10	-0.10	0.14%
RaRe71417	M	6/29/2009	8	-0.10	-0.10	0.14%
SaCo83017	F	6/15/2012	5	0.00	0.10	0.14%
SzEm9117	F	9/18/2012	4	0.00	0.10	0.52%
WiDa62817	F	10/31/2012	4	0.00	0.00	0.27%
WiMi62817	F	1/18/2011	6	-0.10	-0.10	0.14%
ZhJa9117	M	8/10/2012	5	0.10	0.00	0.37%

Chapter 6 CVI Raw Data

ID	Gender	Birthdate	Age at exam	Diagnosis	logMAR 100%	logMAR 50%	logMAR iso
BeVi41317	F	12/9/2009	7	CP, strab, CVI	0.68	1.08	0.58
DeAl41017	F	1/8/2010	7	developmental delay, microcephaly	0.68	1.08	0.58
DeHe6216	F	11/2/2006	9	gross motor delays, S&L disorder, ET	0.20	0.20	0.00
DeSa62217	F	12/7/2006	10	microcephaly	0.68	0.88	0.58
GrLe61716	M	3/23/2011	5	alternating exotropia, PVL	0.00	0.30	0.00
KaAr32917	M	5/15/2009	8	CP and birth asphyxia	0.58	0.78	0.48
LoJo5216	M	9/12/2001	14	premature, drug exposure in utero, shaken baby syndrome, optic atrophy and CVI	1.08	1.38	1.07
MaJa32317	M	5/6/2011	6	minor dysmorphic corpus callosum	0.70	1.00	0.70
McVi91715	F	4/16/2004	13	chromosomal disorder, CP	0.78	0.78	0.48
MiMa71116	F	3/4/2008	8	CP, CVI, VP shunt for hydrocephalus	0.20	0.40	0.10
MoCa81116	F	1/1/1996	20	CP, dev delay, ROP, RD, Cataracts	0.60	0.80	0.60
MuEd72017	M	6/4/2008	9	CVI risk	0.28	0.28	0.28
PrAn12317	F	11/3/2006	10	CP, developmental delay, CVI	0.54	0.70	0.40
RoEt72017	M	9/14/2011	6	PVL	0.18	0.18	0.18
Scls81216	F	1/20/2007	9	seizures	-0.10	-0.10	-0.10
TaSh62317	F	5/23/2002	15	TBI	0.88	0.88	0.78
TeDa91516	M	11/27/2005	10	left hemispherectomy, right hemianopsia	0.20	0.30	0.00
ThAs112816	M	5/24/2008	8	Joubert's syndrome, pre fragile X count 59	0.20	0.20	0.30
WhHa82216	M	9/2/2006	9	premature, high myope	0.40	0.40	0.40

Chapter 6 Ocular Disease Raw Data

ID	Gender	Birthdate	Age at exam	Diagnosis	logMAR 100%	logMAR 50%	logMAR iso
ChGa82916	M	9/7/2004	11	ROP, prog high myopia	0.51	0.80	
ClJa8217	M	4/17/2013	4	achromatopsia and nystagmus	1.08	1.18	1.08
CoMc2817	F	1/23/2012	5	ROP	0.68	0.88	0.68
GaVa72417	F	1/23/2006	11	retinitis pigmentosa	0.68	0.78	0.58
GrAb11416	F	2/19/2009	8	OCA type 1	0.58	0.78	0.58
GrAb121415	F	2/19/2009	6	OCA type 1	0.68	0.78	
KeAn6717	F	9/19/2008	8	ROP/strab	0.10	0.20	0.10
KiGa10314	F	9/6/2009	5	albinism	0.63	0.90	
LaTr52016	F	7/31/2011	4	congenital motor nystagmus and mild ocular albinism	0.40	0.51	0.22
LiLu101316	F	1/11/2010	6	PHPV, OS RD	0.51	0.70	0.40
LoJo71017	M	5/3/2010	7	mutation in gene, asthma, seizures	0.78	0.78	
MaCi11915	F	2/2/2009	6	achromatopsia	0.58	0.70	
MaUr10517	M	9/12/2010	7	former dx of hearing impairment	0.28	0.58	0.28
McAl72814	F	7/2/2010	4	ocular albinism	0.27	0.36	
MnCl51316	F	7/23/2013	3	bilateral retinoblastoma	0.51	0.81	
NePa61616	M	10/8/2010	5	right microophthalmos, right cataract, bilateral colobomas of iris, optic nerve and retina	0.18	0.28	0.08
PfAn11316	F	12/26/2008	7	OCA	0.70	0.80	
PlAm7617	F	5/13/1988	29	RP, Cohen syndrome (dev. Delay), type II diabetes	0.51	0.60	0.51
ReJe62817	M	5/8/2015	2	ocular albinism, infantile nystagmus syndrome?	0.58	0.78	0.58
VaEl82817	F	3/19/2003	14	microophthalmia, chorioretinal colobomas, hearing loss	1.28	1.38	1.28