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QUALITY OF LIFE, READING AND ACCOMMODATION IN CHILDREN WITH LOW VISION

By

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A DISSERTATION

Submitted to the graduate faculty of The University of Alabama at Birmingham
in partial fulfillment of the requirements for the degree of
Doctor of Philosophy

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DAWN KISSNER DECARLO

VISION SCIENCE

ABSTRACT

Childhood permanent, uncorrectable vision impairment (VI) is rare, yet it is a public health burden as the impairment lasts a lifetime. Vision impairment describes decreased vision that affects everyday activities. Acuity cut-points commonly used include 20/40, 20/60 or 20/70. Blindness often refers to legal blindness (best corrected visual acuity of 20/200 or worse or a visual field less than 20 degrees). Children with VI often have hereditary conditions such as albinism, optic atrophy and retinal degenerations and are different in many ways than adults with VI. The majority have conditions with onset at or near birth and as a result also have nystagmus. Despite this, relatively little is known about the best rehabilitation strategies to ameliorate the symptoms caused by VI.

This dissertation focuses on measuring 3 aspects of pediatric VI: quality of life, near focusing (accommodation) and reading. Here we have shown that the PedsQL™ 4.0, a generic health related quality of life instrument, has excellent internal consistency reliability. It has good convergent validity as poorer visual acuity is associated with lower quality of life scores. The PedsQL™ 4.0 can discriminate between samples of children with normal vision and those with VI. Near accommodative accuracy was measured using a gold standard autorefraction method and a quick clinical test. Both tests found greater focusing inaccuracy for children with vision impairment and that the inaccuracy was greater for a 6D demand condition than 4D. Lastly, this work validated the use of the MNREAD for measuring reading in children with VI. Maximum reading

rate and reading acuity had excellent test-retest repeatability. Critical print size showed more variability. The MNREAD test and a paragraph reading test, the Jerry Johns Basic Reading Inventory, were strongly correlated (p=0.88), however reading rates were faster on the MNREAD. Clinicians should be aware that MNREAD testing may over-estimate reading speeds expected for typical reading materials.

The PedsQL™ 4.0, accommodative response testing and MNREAD testing are all valuable tools that can be used to evaluate function in children with VI. They should be considered as potential outcome measures for future studies on rehabilitation in pediatric VI.

Keywords: vision impairment, quality of life, pediatric, reading, MNREAD, accommodative response

DEDICATION

This work is dedicated to all of the children with low vision and their families who so willingly participated in this research. They inspire me with their creativity, humor, kindness and perseverance. It is also dedicated to Alie B. Gorrie whose support of the UAB Center for Low Vision Rehabilitation through Songs for Sight enabled the formation of the Songs for Sight Youth Low Vision Support Group. The support group has facilitated friendships between children and families of children with low vision so that they know they are not alone dealing with the struggles of vision impairment.

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LIST OF ABBREVIATIONS

BPEDS	Baltimore Pediatric Eye Disease Study
cm	centimeter(s)
CPS	critical print size
D	diopter
IQR	Inter-quartile range
logMAR	log minimum angle of resolution
MEM	monocular estimate method
MEPEDS	Multi-Ethnic Pediatric Eye Disease Study
MPS	minimum print size
MRS	maximum reading speed
NEI VFQ	National Eye Institute Vision Function Questionnaire
OD	right eye
OS	left eye
PedsQL™	Pediatric Quality of Life Inventory
PROM	patient reported outcome measure
QoL	quality of life
RA	reading acuity
VI	vision impairment
wpm	words per minute

CHAPTER 1: INTRODUCTION

The educational system in the U.S. relies heavily on reading for learning and for progression to more advanced levels of education. Since reading is a highly visual task, children with irreversible vision impairment (VI) are often at a disadvantage. Most children with VI have enough sight to read visually and do not learn Braille [1]. Currently there are no "standards of care" for treatment of the reading disability caused by pediatric VI, and strategies vary widely by both medical and educational professionals. The main options available to access reading material include use of: close working distances, large print, optical or electronic magnification, auditory means and Braille. There is no evidence-base available to guide clinical and educational decisions about which modality is most appropriate for each individual. In order to build this evidence base, we must first develop methodologies appropriate for CHILDREN with VI to reliably measure aspects of functional vision such as accommodation, reading and vision-targeted health-related quality of life.

The terms low vision and VI are often used synonymously to refer to a condition of reduced visual acuity and/or visual field or to reduced visual function. 20/40, 20/60 or 20/70 are frequently used acuity cut-offs for VI. The World Health Organization uses 6/18 (20/60) [2, 3]. Blindness refers to a state without vision, however legal blindness (in the U.S.) [4] refers to visual acuity less than or equal to 20/200 in the better seeing eye with best-correction, or if the vision is better than 20/200 then the visual field is less than

or equal to 20 degrees in its widest meridian. Thus, legal blindness is a subset of low vision. Sometimes the term blindness is used to mean "legal" blindness, adding to the confusion.

Epidemiology and Public Health Burden

Many people have never met a child with VI since pediatric low vision is rare. Scientific information about its prevalence is scarce and difficult to obtain. Foster and Gilbert [5] used data from blind registries in Europe and population based surveys in Asia and Africa to develop an algorithm to estimate prevalence rates of childhood blindness based upon mortality rates for children under 5. Gilbert et. al. [6] suggest that the rate is approximately 0.1/1000 children aged 0-15 years in the wealthiest countries. Using Foster's algorithm, Muñoz and West [7] estimated the rate in the United States and Canada to be 3/10,000 for a total of 20,100 estimated blind children. The Metropolitan Atlanta Developmental Disabilities Surveillance Program determined the rate of VI and blindness (vision 20/70 or worse) in Metropolitan Atlanta in children aged 6 to 10 between 1991 and 1994 to be 10.7 per 10,000 children [8]. There were no statistically significant differences in rates between races or genders.

More recently, population-based studies have been conducted in the United States. The Multi-Ethnic Pediatric Eye Disease Study (MEPEDS) evaluated African-American and Hispanic children [9] as well as Asian and non-Hispanic white children [10] aged 30 to 72 months in Los Angeles, California. Vision was assessed through a standardized comprehensive eye examination. Of 3,364 African American and Hispanic children there were only 4 with better eye vision impairment due to ocular disease. An

additional 17 had confirmed bilateral amblyopia. There were no cases of bilateral, non-refractive or amblyopic vision loss in children of Asian descent (n=939) and only one out of 947 non-Hispanic white children with better eye VI. Similarly, the Baltimore Pediatric Eye Disease Study (BPEDS) [11] using the same study protocol as MEPEDS found that 4 of 1347 children had VI in their better eye due to ocular disease. Combining the MPEDS and BPEDS data, the prevalence of pediatric VI is approximately 13.6 per 10,000 children. Bilateral amblyopia affects an additional 33.3/10,000 preschoolers based upon these 3 studies. Data from the National Survey of Children's Health suggests there were 840,922 children in the US with parent reported vision not correctable with glasses or contact lenses in 2012 [12]. On January 4, 2016, there were 39,471 children who were on the American Printing House for the Blind, Inc. registry as eligible for federal quota funds (children must be legally blind to be eligible) [13], but this number does not count those children with low vision who are not legally blind. Some studies do find differences in rates between genders, presumably due to x-linked recessive genetic eye conditions [1].

Although children represent a small proportion of visually impaired or blind persons in this country when compared against the older adult population, they represent a significant public health issue due to the number of life-years affected when VI begins in infancy [14, 15]. In 1996 it was estimated that the global financial cost of childhood blindness (defined according to the World Health Organization – best corrected vision of 20/400 or worse) in terms of loss of earning capacity is between US $6 trillion and $27 trillion, surpassing the cost of adult blindness [14]. Most of this loss occurs in high-income countries where the prevalence is lower, but children live longer and have greater

earning capacities. In fact, only cataract ranks higher than childhood blindness on the global burden of eye disease when measured in disability adjusted life years, also known as DALYs [16]. The economic burden in 2012 for children ages 0 to 17 in the U.S. was estimated to be $5.9 billion [17].

Differences Between Adult and Childhood Onset Vision Impairment

Causes of VI and blindness in children vary greatly from those in adults. In 5 studies conducted in the United States, primarily in schools for the blind, optic atrophy, cataract, albinism, retinopathy of prematurity, cortical VI and retinal degenerative disease were common causes of VI [1, 18-21]. The underlying etiology of many of these conditions is genetic. Sometimes the VI is part of a genetic syndrome [20]. Birth trauma (e.g. hypoxia), premature birth and intrauterine factors (e.g. maternal exposure to toxins) may also lead to congenital VI. Acquired VI in children may be due to trauma, tumor (brain or ocular), or later onset hereditary conditions.

Another difference between children and adults with low vision is that there is a high prevalence of nystagmus in children with congenital VI, whereas nystagmus is almost never present in adults with acquired impairment. Nystagmus refers to involuntary, typically conjugate, often rhythmic oscillations of the eyes. The term congenital nystagmus is often used synonymously with infantile nystagmus syndrome; however, it is technically incorrect as nystagmus does not typically develop at birth but more likely at 2–3 months of age. Infantile nystagmus may be associated with retinal or optic nerve maldevelopment (previously known as sensory nystagmus) or may occur in isolation (previously known as congenital motor nystagmus). Infantile nystagmus has

several common associated findings: pendular progressing to jerk waveform, associated strabismus and refractive error, decreasing amplitude/frequency with convergence and the presence of a null zone [22]. Figure 1 shows a typical waveform for a patient with oculocutaneous albinism. There also may be an associated head posture or latent

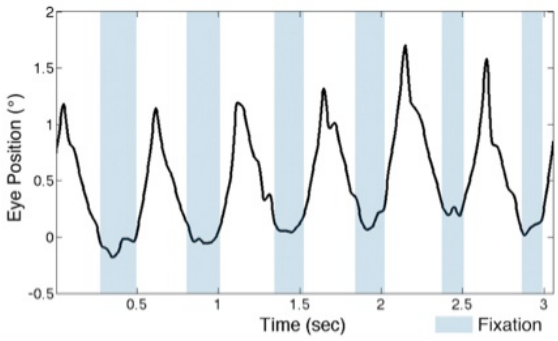

Figure 1: Eye movement recording for a patient with nystagmus due to oculocutaneous albinism. Blue bars indicated foveation periods.

component. Correlations exist between increasing amplitudes and/or frequencies of nystagmus and decreasing distance visual acuity due to shorter duration of foveation (better acuity is associated with longer foveation times) [23]. It has been suggested that the dampening of the nystagmus in near gaze also promotes better near vision, however in well-controlled studies, there was no improvement between distance and near acuity, even when the nystagmus slowed considerably [24-26]. It is also important to note that children with infantile nystagmus do not perceive the world as moving [27, 28] and do not show evidence of significant motion smear [29].

Children with VI also tend to have more refractive error than their peers. Du, et al. [30] reported a normal distribution of refractive error among 813 children with VI, as opposed to the leptokurtic distribution seen in children with normal vision. They found a tendency toward hyperopia while Nathan et al.[3] found a tendency toward myopia among

children with vision impairment. Another study found that albinism, but not foveal hypoplasia alone was associated with increasing hyperopia [31]. The frequency distribution of spherical equivalent (sphere power + ½ cylinder power) refractive error in the right and left eyes among children seen in a low vision clinic is shown in figure 2 [32]. The spherical equivalent values were not normally distributed. Emmetropization is the process whereby the eye avoids ametropia. The mechanism is not fully understood, but involves both feedback on retinal image focus and genetic processes. A high prevalence of ametropia as well as a normal distribution suggest a failure to emmetropize among children with vision impairment.

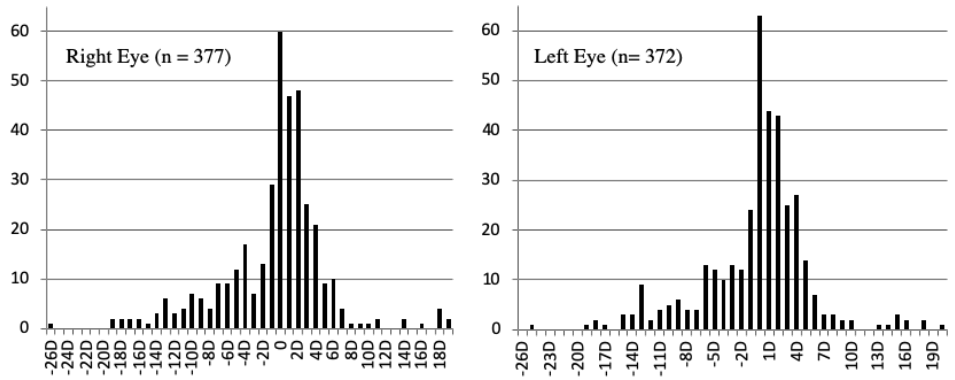

Figure 2: Frequency distribution of spherical equivalent refractive error of children with vision impairment seen in UAB Center for Low Vision Rehabilitation.

Vision-Specific, Health-Related Quality of Life

Quality of life (QoL) is a holistic concept that has no physical or temporal basis and as such it is not directly measurable [33]. Koot [34] suggests that at a minimum, physical, emotional and social domains be addressed in the study of quality of life. These constructs were evaluated through the use of focus groups of children with VI ages 5 to 12 and their parents [35]. The focus groups were conducted in separate rooms by trained

facilitators using a structured script. Psychosocial aspects of VI and school-related issues were in the top three for negative comments for both parent and child focus groups (Figure 3). The findings of these focus groups helped to inform the choice of quality of life instrument used in this work.

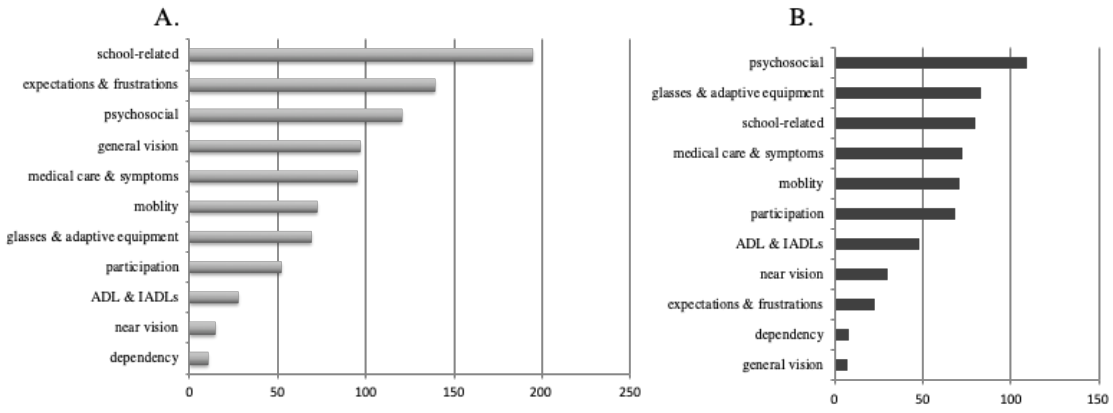

Figure 3: Numbers of negative (problem)comments by focus group topic areas. A.) parent focus groups (gray bars) and B.)child focus groups (black bars). Note: reprinted from "Impact of pediatric vision impairment on daily life: Results of focus groups" by D.K. DeCarlo, G. McGwin, Jr, M.L. Bixler, J. Wallander and C. Owsley. Optometry and Vision Science, 89, p. 13-14. Copyright 2012 by Wolters Kluwer Health, Inc and Copyright Clearance Center. Reprinted with permission.

The National Eye Institute Vision Function Questionnaire (NEI VFQ) was designed to assess vision-specific health-related QoL across a range of chronic eye diseases in adults [36-42]. It has become the gold-standard for QoL measurement in adults with eye disease. However, many questions, for example those about driving, do not apply to children. So, although the NEI VFQ has become widely accepted in eye care research, it is not suitable for use with children.

There is a significant movement in the field of pediatric QoL research to pair disease or function specific modules with generic QoL instruments. By using a generic

measure, QoL can be compared across disease states. Surveys that assessed multiple domains of health-related QoL and that were designed for use in children ages 5-18 were reviewed. Those surveys that were available in both child and parent proxy report forms and had acceptable psychometric properties were given highest consideration for use in this research. Three finalists were identified: the Child Health Questionnaire,[43, 44] the DISABKIDS project [45] and the Peds QL 4.0 [46-48]. The Child Health Questionnaire, Child form has an emphasis on behavior problems (e.g. lying, cheating) not typical in children with VI and thus it was not chosen for this project. The DISABKIDS Chronic Generic Measure-37 simply does not cover the age range we plan to study and therefore also was not chosen.

The PedsQL™ (Pediatric Quality of Life Inventory™) is designed as a modular system, with a generic core scale and disease specific modules [49]. The main advantage is that the generic core scale can be compared across health conditions as well as to healthy populations. It is a 23-item measure designed to address physical, social, emotional and school functioning. The PedsQL™ 4.0 has been shown to have adequate internal consistency reliability (Cronbach's α ranging from 0.68 to 0.88 for child forms and 0.75 to 0.99 for parent forms [46]. The PedsQL™ 4.0 was also able to distinguish between healthy children and those with acute or chronic conditions and was related to indicators of morbidity and illness burden [46].

The PedsQL™ 4.0 has forms for child self-report for ages 5-7, 8-12 and 13-18. Parent proxy report forms are available as well, plus a form for ages 2-4. Several disease-specific modules are available including asthma [48], rheumatology [50], diabetes[51], cancer [52] and cardiac conditions [47]. The PedsQL™ 4.0 generic core scale is an

excellent QoL measure as it has been thoroughly validated, tested in many chronic health conditions, has developmentally appropriate versions to accommodate different ages, is short and easy to administer and has both parent and child report forms. Scores on the PedsQL™ 4.0 range from 0 to 100 with 100 being a state of perfect health.

Investigators have also sought to develop a QoL measure for children with VI, however, none has emerged as a standard for evaluation of QoL in this population. The Effects of Youngsters' Eyesight on Quality of Life questionnaire was developed specifically for use in children with juvenile arthritis-associated uveitis[53, 54] and addresses issues not typical for children with non-inflammatory-related vision impairment. The Children's Visual Function Questionnaire is a parent-report only instrument for children up to age 7 [55]. The LV Prasad Vision Function Questionnaire was designed as a screening tool for use in developing countries. This questionnaire measures only vision function and does not address domains involving social, emotional or school functioning [56]. The Impact of Vision Impairment for Children questionnaire [57] was developed in Australia for children ages 8 to18 and addresses many psychosocial and school related issues addressed more generally by the PedsQL 4.0.

There have been a few small studies looking at groups of children with specific ocular conditions. One study (n= 38) used the PedsQL 4.0 to assess QoL in children with inherited retinal conditions [58]. Overall, the scores were low (Total score 65.5 ±16.7), Physical Health Score 65.1 ±20.3 and Psychosocial Health Score 65.7 ±16.4) for Child report and Total score 60.6 ±17.9, Physical Health Score 59.4 ±21.6 and Psychosocial Health Score 62.0 ±17.0. The participation rate was low (29%) so there may have been selection bias. Additionally, since the survey was mailed to families, it cannot be

guaranteed that the child independently completed the survey. As many inherited retinal conditions are progressive (precise diagnoses were not given), fear of further loss of vision may have also contributed to low scores.

A study of congenital cataract used 2 QoL measures (PedsQL 4.0 and the Impact of Vision Impairment for Children questionnaire[57]) as well as a functional vision assessment (Cardiff Visual Ability Questionnaire for Children) [59]. They evaluated 72 children with congenital cataracts of whom 60% (n=43) were bilateral. The median best-corrected visual acuity was 0.18 logMAR (IQR 0.02-0.43), but these were children who had become aphakic, pseudophakic or had developed secondary glaucoma, so visual acuity alone does not adequately represent their visual status. The participants had reduced QoL as measured by both instruments. Interestingly, the decrease in QoL associated with congenital cataracts on the PedsQL 4.0 was similar to that experienced in pediatric liver transplant patients. Another study in children with glaucoma found that decreased acuity, bilateral involvement and multiple surgical procedures were associated with poorer QoL [60].

Accommodation in Pediatric Vision Impairment

Accommodation refers to the involuntary process of changing the shape of the physiological intraocular lens that induces a power change which brings an object of interest into focus on the retina. Accommodation is a complex process that is neurologically intertwined with convergence and pupillary constriction. Information is sent from the photoreceptors through the retinogeniculocortical pathway presumably providing blur information to neurons in the temporal and frontal cortex that likely

project to the supraoculomotor area of the midbrain, located dorsal and lateral to the oculomotor nucleus. These inputs are not fully understood. These neurons project to the Edinger-Westphal nucleus which provides the primary drive for accommodation and pupillary constriction. They also project to medial rectus motoneurons to produce convergence. Input likely also comes from an area near or including the nucleus of the posterior commissure. Additionally, cells in the frontal eye fields have been shown to be related to ocular accommodation [61]. Afferent fibers from the Edinger-Westphal nucleus travel with the oculomotor nerve to synapse in the ciliary ganglion and then through the short ciliary nerve to the iris sphincter muscle to decrease pupil size or to the ciliary body to affect accommodation. Some fibers go directly to the medial rectus muscle to stimulate convergence without synapsing in the ciliary ganglion [62].

Once the ciliary muscle is stimulated to contract, the biomechanical changes that increase lens power begin to occur. As the ciliary muscle contracts, it moves inward and anteriorly. This action releases tension on the anterior lens zonules which in turn allows the elastic properties of the lens capsule and the viscoelastic properties of the lens itself to enable the lens to assume a more spherical shape (which produces more plus power) [62].

Children with VI tend to hold reading materials much closer than other children (the object's image on the retina is larger when it is held closer) as a primary means to compensate for their vision impairment. Reading at closer distances requires more accommodative effort. The accommodative demand (diopters) is the reciprocal of the test distance in meters; at 25cm 4D of accommodation is required whereas at 5cm 20D is needed. Thus, if holding objects closer is a rehabilitation strategy for reading that is encouraged for visually impaired children, it is important that they have adequate

accommodative ability to maintain focus at that distance. If there is anomalous accommodation, then remediation with lenses and/or vision therapy can be part of the rehabilitation strategy.

Experts agree that blur is a stimulus to accommodation [63-66]. It is well established that myopes interpret and adapt to blur differently than emmetropes [67-70]. Ciuffreda et al [71] found that blur sensitivity decreased with increased target size in participants with normal vision. Chung and Bedell [72] demonstrated that some low vision observers show higher tolerance to blur. Given that accommodation is driven by blur detection [73] it would be logical to expect that VI may affect accommodative accuracy. In one study [74] 10 participants with VI due to congenital nystagmus (isolated or associated with albinism) between ages 17 and 30 had their accommodative accuracy measured using a Hartinger coincidence-optometer. The accommodative error of the nystagmats was 50% greater than the normal controls. Perhaps owing to the small sample size, the differences were statistically significant (t-test, <0.01) only at stimulus levels of 1,4 and 6 diopters.

Many additional factors are known to affect accommodative response including vergence, proximity and chromatic aberration [66]. Factors that contribute to depth of focus (the distance the image is in front of or behind the retina before defocus is apparent), such as target contrast [75], spatial frequency[76], luminance [77] and pupil diameter [78]can vary significantly before there is any effect on accommodation. Ciuffreda's work [76, 79, 80] has demonstrated that amblyopic eyes show reduced static accommodative response to broadband stimuli. They also found that the increased depth of focus generally found in eyes with amblyopia cannot account for most of the

accommodative loss. He proposes that a gain loss in the accommodative system is responsible for the reduction in accommodative response magnitude.

According to Ciuffreda [73] the accommodative system is much more sensitive to the effects of target retinal eccentricity [81] and retinal-image motion [82]. The latter two are likely to affect accommodation in vision impairment due to central scotomas and/or nystagmus in addition to the effects of the acuity impairment.

The accuracy of near focus (measured in diopters) is called the accommodative response. It is the difference between the accommodative demand required to perfectly focus a target and the amount of accommodative effort actually used to focus that target. If more effort is exerted than is necessary to achieve perfect focus, it is termed a lead of accommodation whereas less effort is termed a lag of accommodation. Dynamic retinoscopy is used to measure accommodative response and can be performed by a clinician or with the use of an autorefractor. There are two methods for dynamic retinoscopy performed by clinicians: monocular estimate method (MEM), which uses lenses to focus the reflex and Nott in which the clinician moves the retinoscope to focus the reflex at the far point. Automated measures of accommodative response use an open-field autorefractor so that the target can be presented in free space at a distance determined by the examiner.

Leat and Gargon [83] using Nott retinoscopy found that children ages 3 to 10 had inter-observer repeatability within 0.5D, and that the mean across all age groups was 0.48D (+/-1D, 95% confidence limits), although from ages 11 to 26 the mean lag increases with accommodative demand. Rouse et. al. [84] using MEM retinoscopy measurements taken at the child's habitual working distance (average 35cm +/- 7cm or

2.86D accommodative demand) found mean lags of accommodation of +0.33D OD and +0.35D OS. McClelland and Saunders [85] using Nott retinoscopy studied 125 school aged children from 4 to 15 years of age and using regression analysis found no difference in accommodative response between age groups, but that the accommodative lag did increase with stimulus demand (0.30 +/- 0.39 at 4D, 0.74+/- 0.58 at 6D and 2.50 +/-1.27 at 10D).

Assuming equal testing conditions (target size, test distance, contrast) there is no a priori reason to expect differences in accommodative response measurements between these methods [86-88]. Accommodative response measured by both MEM and Nott has been shown to have high correlation with automated measures [89-91]. However, the COMET-2 study found that accommodative responses in myopic children using the Grand Seiko WR 5100K showed a greater lag of accommodation than Nott or MEM dynamic retinoscopy. They could not identify a cut-point using receiver-operator curve analyses with either type of dynamic retinoscopy to achieve adequate sensitivity and specificity to detect a 1D or greater lag of accommodation as measured by the Grand Seiko [92].

Automated measurement is the preferred method of assessing accommodation in large scale studies of refractive error in children [93, 94], however automated measurement of accommodative response may not be obtainable in all patients with nystagmus. This equipment requires considerable cooperation from the child and steady fixation, which cannot always be obtained when there is nystagmus present. In a small pilot project, Heyman and colleagues [95] examined 10 children with congenital macular

disorders and were able to measure accommodative response using the Grand Seiko WV500 Autorefractor demonstrating that automated testing is possible in this population.

Accommodation has been studied in some groups of people with vision impairment. Reduced accommodative response has been shown in small numbers of subjects with albinism [96], juvenile macular degeneration [97], congenital nystagmus [74] and achromatopsia[98]. Reduced accommodative response has also been shown in amblyopia [76]. In the largest study to date, Leat and Mohr [99] examined the accommodative response of 21 pre-presbyopes with low vision (aged 3 to 35 years) and found that 85% were outside the 95% range of normal and that the errors were often more than predicted by the increased depth of focus due to their low vision. Possibly owing to their small sample size, no statistical associations were found with visual acuity, age, nystagmus (presence or absence) or refractive error. They conclude that this reduced accommodation may have important clinical implications in the rehabilitation of young people with vision impairment.

Reading in Pediatric Vision Impairment

Reading is a critical task for education and much of our learning depends upon it. If we are unable to read, or unable to read at an ability level similar to our peers, we are unlikely to be able to succeed educationally. Reading translates into literacy, an essential skill with life-long quality of life implications. Low literacy levels are strongly associated with lower socioeconomic status [100]. As such, reading has important implications for both education and employment.

In a study of 185 visually impaired students in Tennessee, Corn et. al. [101] found that average silent reading rates (which are typically faster than oral reading rates) by grade prior to intervention with low vision devices were less than 100 words per minute across all grades (see figure 4). The reading speeds in this study were measured using an educationally based test, the Burns and Roe Informal Reading Inventory [102]. Using Carver's normative data [103] compared to their data on children with VI, Corn and colleagues reported that second graders start out with silent reading rates about 50% below their peers and this lag is maintained through elementary school, after which the gap widens (because school-age children with VI in her study on average, plateaued under 100 words per minute by 6th grade). In terms of workload, it would take the average visually impaired 2nd grader twice as long to read the same assignment, assuming they had the stamina to do so, and this discrepancy in time to complete a reading task only increases in higher grades. It is easy to see then, how deleterious VI could be to education.

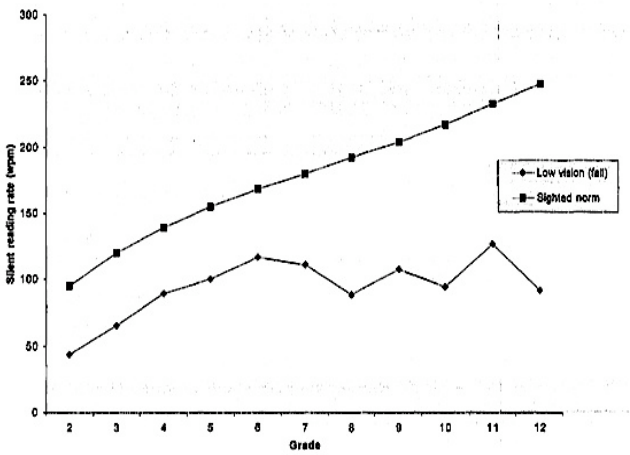

Figure 4: Average reading speed by grade for children with low vision and for national normative data. Note: From "An initial study of reading and comprehension rates for students who received optical devices" by A.L. Corn, R.S. Wall, R.T. Jose et.al., Journal of Vision Impairment and Blindness, 2002, 96, 322-334. Copyright 2002 by SAGE Publications. Reprinted with permission.

Most children with VI have enough sight to read visually and do not learn Braille [1, 104]. A consistent finding of studies of reading rate in children with VI is that they are on average slower readers than their peers. Two studies found that reading rates did not exceed 100 wpm for any age group and that differences in reading speed between children with and without VI increased with increasing age [105, 106]. Of all studies found after an exhaustive literature search, the fastest mean maximum oral reading rate reported in a study of children with VI is 147 ± 61 words per minute (wpm) [107]. The reading rate increased by 9.9 wpm per year of age, in contrast to normative data from Carver [108] where the reading rate of children with normal vision increased by 14 wpm per year of age. Because reading rates will vary depending on many factors (age and grade of child, text size, difficulty, length, mode of presentation, type of reading: oral versus silent, skimming versus reading for comprehension, also known as rauding), there is no gold standard "normal" reading rate for children or adults. Studies using a sighted control group provide the best comparisons, as the testing situations are the same. A study conducted in the Netherlands examined both children with normal vision and with vision impairment who had between 40 and 60 months of education. The low vision readers were slower on both single word (75.4 ± 21wpm) and continuous text reading (54.4 ± 17.9 wpm) than their age matched peers who read 87.6 ± 18.3 wpm for single words and 83.1 ± 25.0 wpm for continuous text [109]. Rice and colleagues found that normally sighted readers aged 8 to 18 (median 11) had mean maximum reading speeds of 177 ± 46 wpm, while children with vision impairment (age range 10-12) read more slowly at 140 ± 29 wpm [110].

Other studies have also reported slower reading rates for children with vision impairment [105, 106, 111, 112]. Douglas and colleagues [105] found reading accuracy, comprehension and speed in a large sample of children with vision impairment in Great Britain to lag behind their normally sighted peers. Mean oral reading rates did not exceed 100 wpm for any age group and differences in reading ability (accuracy, comprehension and speed) increased with increasing age. In a follow-up study, they matched 25 low vision readers to 25 normally sighted readers based on reading ability and found that on average the normally sighted readers were almost 2 years younger than those with vision impairment [113]. They also determined that children with vision impairment were more likely to make substitution errors than mispronunciations, whereas the reverse is true in children with normal vision.

In a study of adults with congenital VI, maximum reading speeds were 18.8% slower in participants with albinism and 14.7% slower in those with idiopathic infantile nystagmus when compared to controls [112] suggesting that this limitation in reading speed is not simply a delay in development. Studying reading rates in children is more complex than in adults, as reading rates continue to develop among normally sighted children even through college [108]. Legge points out that the blend of developmental factors in perception and cognition that underlie the gradual development of reading speed are unknown [114].

Much of what we know about the visual requirements for reading comes from a series of papers on adults by Legge and colleagues known as “Psychophysics of Reading”[115-131]. From their work on adults, we know that in normal vision, maximum reading rates are achieved for characters subtending 0.3-2 degrees of visual

angle and that there is a gradual decline for letters larger than 2 degrees, possibly due to speed limitations in the smooth-pursuit eye-movement system. Additionally, they demonstrated that at least 4 letters must be simultaneously visible, or reading speed will slow [123]. There is wide variability in reading performance among adult low vision readers, most of which can be accounted for by the status of the central field and media [128].

Legge and colleagues [132] translated their basic research on reading and vision and developed the MNRead test. Once developed, a chart-based version was created [132] to use as a simple to administer test for both research and clinical care. MNREAD has print sizes from logMAR -.5 to 1.3 (corresponding to Snellen 20/6.3 to 20/400), for a standard reading distance of 40 cm with 0.1 logMAR steps between sentences. The print (font style, character and line spacing) is similar to what one would encounter in ordinary reading tasks. MNREAD is based on a restricted vocabulary of common words the majority of which were in the 1000 most frequent words in third grade school books.

There are many tools (primarily used by educators) that can be used to measure reading speeds such as the Dynamic Indicators of Basic Early Literacy Skills test [133], the Basic Reading Inventory [134] or the Burns and Roe Informal Reading Inventory [102], however these tests are impractical for clinical use and measure only reading speed. The MNREAD is the only clinical test that is commercially available to measure reading speed at multiple print sizes. Classic near vision tests measure only the near acuity. Legge developed the concept of the Critical Print Size or the smallest print size at which maximum reading rate is achieved. Reading acuity is the smallest size print resolvable. Reading rate slows rapidly as the reading acuity is approached. Critical print

size therefore, could be used to objectively determine print size recommendations and device prescriptions for use in the educational setting.

There are no psychometrically validated tests for use with children with VI to determine reading acuity/rate or critical print size. The MNRead determines (among other things) the Critical Print Size, or smallest print size read at maximum reading rate as well as the reading acuity (minimum print size) and reading rate. Reading acuity/rate would be a primary outcome measure for any future trials of interventions for reading rehabilitation for children with vision impairment, therefore it is important to investigate the performance of this test in that population.

The MNRead charts have been validated for use in adults with both normal and low vision [132]. Virgili, et. al. [135] used an Italian version of the MNRead in 116 normally sighted, non-dyslexic children grades 3 to 8. Test-retest means were not significantly different from each other for reading acuity (logMAR), Critical Print Size (logMAR) or maximum reading speed (log words per minute). They confirmed that the reading speed across sentences of sizes above the Critical Print Size was stable and that the small difference was clinically insignificant. Additionally, the internal consistency of the Italian charts was high with respect to reading speed measurements (chart 1 $\alpha = 0.96$, chart 2 $\alpha = 0.97$). Recently work has been undertaken in Legge's laboratory to validate and establish norms for the MNRead in children with normal vision as young as 8 years of age [136, 137]. Critical print size (logMAR) was 0.06, 0.03, 0.03 and -0.01 Maximum reading speeds (words per minute) were 145, 151, 165 and 193 for grades 3,5,7 and adults, respectively [136]. Thus, children with normal vision as young as 8 years old and 3rd grade are able to perform this test. Although reading speeds are slower in children

with VI, there is no reason to expect that they would be unable to perform this test if they meet the standards for cognition that we set. Thus, there is ample evidence that the group we propose to study will have the ability to perform the test. Rice, et. al. [138] studied children aged 8 to 15 with and without vision impairment and used an abbreviated protocol where only 3 large paragraphs are read to determine if maximum reading speed could be determined without administering the entire MNRead test. They found that the abbreviated protocol produced reading speeds that were nearly identical to standard administration of the MNRead. This method, however gives only reading speed, not critical print size or minimum print size, two values of major interest in this proposed project. Additionally, we will evaluate two testing conditions and compare them to an educationally based test to determine if either or both conditions are appropriate clinical measures for recommending print size to use in the classroom.

CHAPTER 2: SPECIFIC AIMS

As detailed in the introduction to this dissertation, pediatric VI is a low incidence problem. Because of the low incidence and varied causes, it is difficult to obtain a large number of participants for clinical research. Much of the research on this population suffers from small sample sizes and therefore a lack of statistical significance. This is evidenced by two Cochrane systematic reviews. The first examined optical reading aids in pediatric VI [139] and concluded that there was a "lack of good quality evidence regarding the use of optical low vision aids in children and young people." The second examined assistive technology for the same population [140] and found that there was not a single randomized controlled trial on this topic. Both reviews emphasized the need for high quality evidence for how health care providers and educators manage vision impairment in children. An additional review of low vision rehabilitation in children [141] noted that "most studies are descriptive case series with small sample sizes, making the science in this field very rudimentary."

To that end, this work was designed to lay the foundation for future research to elucidate best practices for treating VI in childhood. Before a clinical trial could be planned, it was important to validate measures for use in children with vision impairment. As a clinician-scientist, the aims were developed based upon observations seen in my clinical practice which has a heavy emphasis on pediatric VI.

Specific Aim 1: To evaluate the reliability, and validity of a previously established measure of pediatric quality of life, the PedsQL™ 4.0, in children with vision impairment. Given the importance of patient centered outcome measures in clinical research, it is important to establish a tool to measure QoL in pediatric vision impairment. Focus groups[35] conducted in our lab supported the use of the PedsQL™ 4.0 as it has domains that cover the primary concerns of both parents and children. Using this instrument has the additional value of being able to compare the impact of VI to that of many other chronic health conditions of children.

Specific Aim 2: To characterize the focusing accuracy (accommodative response) of children with VI and to compare their accommodative accuracy to that of children with normal visual systems. Accurate near focus is important for reading, since defocused letters will be more difficult to discern. Most children with VI compensate for their decreased acuity by holding reading materials closer (utilizing relative distance magnification – the retinal image is larger when the object is closer). This strategy for compensating for decreased acuity will be less effective in visually impaired children with accommodative dysfunction. There is currently little data available on this subject in children with VI and testing of accommodation is often not performed when clinically assessing these children.

Specific Aim 3: To determine the repeatability and construct validity of the MNRead, a reading acuity and reading speed test, developed and validated for use with adults, in visually impaired children. The MNRead determines (among other things) the Critical Print Size, or smallest print size read at maximum reading rate as well as the reading

acuity (minimum print size). Reading acuity/rate would be a primary outcome measure for any future trials of interventions for reading rehabilitation for children with vision impairment, therefore it is important to investigate the performance of this test in that population. Internal consistency of the charts (Cronbach's alpha) as well as test-retest repeatability will be measured. Construct validity will be evaluated by comparing MNRead reading speeds to a standardized educational test, the Basic Reading Inventory [134].

CHAPTER 3

RELIABILITY AND VALIDITY OF THE PEDSQL™ 4.0 GENERIC CORE SCALES IN PEDIATRIC VISION IMPAIRMENT

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Abstract

Purpose: The PedsQL 4.0 is a generic health-related quality of life (HRQoL) instrument that has been used across many pediatric health conditions. We hypothesized that this instrument would be valid for use in children with vision impairment (VI) and that it could distinguish between children with VI and normally sighted children.

Methods: 70 children with VI and 44 age matched controls underwent vision testing including binocular best corrected distance visual acuity. They completed the PedsQL 4.0 Generic Core Scale Child Report (ages 8-12) or Teen Report (ages 13-18) as appropriate. Parents completed the Parent Proxy Report in a room separate from their child. Analyses included descriptive statistics, intra-class correlations, t-tests and determination of Cronbach's Alpha for subscales.

Results: Groups were similar with regard to age, race and gender. PedsQL subscales did not show any floor effects in this population, however some scales did have ceiling effects of up to 28% in certain groups. Cronbach's Alpha was excellent ($\geq$0.88) for all subscales and reports. PedsQL Total Score for children with VI was significantly different than the score for children with normal sight for both age groups and for both parent and child report. The Total score was also significantly associated with visual acuity. Parent and child reports correlated poorly (ICC<0.5), showing the importance of obtaining both perspectives.

Conclusions: The PedsQL 4.0 is a valuable instrument that can be used to assess HRQoL among children and teens with low vision. It has internal consistency reliability as well as discriminative validity.

Introduction

Pediatric vision impairment (VI) is a low incidence condition, however it is of public health significance owing to the number of life years affected when VI begins in childhood. Vision impairment from ocular disease was rare in both the Multi-Ethnic Pediatric Eye Disease Study [1] and the Baltimore Pediatric Eye Disease Study [2]; each study found a prevalence of 0.1%. Data from the National Survey of Children's Health suggests there were 840,922 children in the US with parent reported vision not correctable with glasses or contact lenses in 2012 [3]. The most common causes of VI and blindness in children are different from those in adults. In 5 studies conducted in the United States, optic atrophy, optic nerve hypoplasia, retinopathy of prematurity, cataract, albinism, cerebral VI and retinal degenerative disease were the most frequent causes of pediatric VI [4-8].

Quality of life (QoL) is an important measure of the impact of VI. It is intuitive that VI would affect QoL, and there are many studies evaluating QoL as it relates to VI in adults. In adults, health related QoL instruments such as the SF-36 [9] did not adequately capture the impact of VI. Therefore several instruments were developed to address vision-specific, health related QoL, the most widely known being the NEI-VFQ [10]. Although there are vision-specific QoL measures for children with VI, none offer both parent and child reports. The Children's Visual Function Questionnaire (CVFQ) is a parent proxy-report instrument designed for children up to age 7 [11]. The Impact of Vision Impairment for Children(IVI-C) [12] uses child self-report but has no parent report.

Previously we reported on focus groups of children with VI and their parents about QoL [13]. After review of the transcripts we determined that the PedsQL™ 4.0 Generic Core Scales were appropriate for use in pediatric VI as they covered the domains most frequently mentioned in those focus groups. It is a 23-question instrument with age-appropriate forms that yields a Total score, Physical Health Summary score (8 items, equivalent to the Physical Functioning subscale) and Psychosocial Health Summary score (15 items, based on the Emotional Functioning subscale [5 items], Social Functioning subscale [5 items], and School Functioning subscale [5 items]). It also has both child and parent report forms, which is important as we found that parents and children had different perspectives of the impact of VI. Importantly, the PedsQL™ 4.0 has been widely used across many chronic conditions of children so that comparisons can be made across conditions.

The objective of this study was to examine the internal consistency reliability and construct validity of the PedsQL™ 4.0 Generic Core Scales in children with VI. We hypothesized that the PedsQL™ 4.0 Generic Core Scales could distinguish between children with VI and those with normal sight (discriminant validity) and that poorer visual acuity would be associated with lower health-related QoL (convergent validity). Additionally, we sought to determine if the differences in concerns reported in our focus group study would manifest as differences in scores between parent and child reports.

Methods

This study was approved by the University of Alabama at Birmingham Institutional Review Board (IRB). A partial HIPPA waiver was granted by the IRB to

obtain personal health information for screening and recruitment of participants. After thorough discussion of the study, all parents and children provided written consent or assent as appropriate for participation. Parents also authorized disclosure of health information for research.

Vision Impairment Sample

Patients and their parents/guardians (hereafter referred to as parents) were recruited from the clinical low vision rehabilitation practice of one of the authors (DKD). Eligible patients were identified through record review. Eligibility criteria included ages 8 to 18 years with best-corrected visual acuity between 20/40 and 20/800, inclusive and ability to speak and understand English. Children with vision less than 20/800 were excluded as they utilize non-visual means for many activities such as reading and mobility and therefore function very differently than children with low vision. Children with co-morbid conditions including intellectual disability were not eligible. Parents of eligible children were sent letters telling them about the study. Approximately 2 weeks later a study coordinator contacted parents by phone and those that were willing to participate in the study were scheduled for a study visit.

Normally Sighted Sample

Children without VI were recruited by means of a flyer placed in the clinic waiting room. Parents of potential participants contacted the study coordinator and were scheduled for a study visit if they reported normal vision and denied other disabilities. Many of the children enrolled were siblings or friends of children with VI. Once in the study, participants were confirmed to meet the following entry criteria: (a) Free of ocular disease as determined by dilated eye health evaluation (b) 20/25 (logMAR 0.1) or better

acuity in each eye, best-corrected (c) Refractive error between +4D and –4D with no more than 2D astigmatism or 0.75D anisometropia (d) Normal stereopsis.

Characterization of Vision

Parents provided demographic and health information including gender, race, history of premature birth, whether or not they were receiving special services in school, the type of school setting they attended (public, private, homeschool or school for the blind), whether or not they had repeated a grade and the gender and marital status of the parent informant. All participants had their best-corrected vision measured in each eye individually as well as using both eyes together using the EVA Tester (Jaeb Center for Health Research, Tampa, FL). Results were recorded as a score code and converted to logMAR. The Slosson Intelligence Test-revised 3rd edition [14] using the supplementary manual for use with the blind and visually impaired [15] was administered to all participants. At the end of the visit, participants were dilated and their ocular diagnosis was confirmed (including the absence of abnormalities for those in the control group).

Administration of the PedsQL™ 4.0 Generic Core Scales

The PedsQL™ 4.0 Generic Core Scales assess health related QoL over the past month. Responses are on a 5-point scale (0 = never a problem; 1 = almost never a problem; 2 = sometimes a problem; 3 = often a problem; 4 = almost always a problem). Items are reverse scored and linearly transformed to a 0 to 100 scale (0 = 100; 1 = 75; 2 = 50; 3 = 25; 4 = 0) with higher scores indicating a better QoL.

The PedsQL™ 4.0 Generic Core Scale child report (ages 8 to 12) and teen report (ages 13 to 18) was administered to participants with normal and with impaired vision in a separate room without their parent present. Children could read and independently

answer the questions if they chose, however if the child had difficulty seeing the survey or reading it a trained coordinator was present who would read the survey to them. Parents self-administered the age-appropriate parent proxy form for their child.

Statistical Analyses

Statistical analyses were conducted using SAS 9.0 (Cary, NC). Demographic data was analyzed using descriptive statistics. Differences between participants with and without VI on demographic characteristics were compared using independent sample t-tests. Internal consistency reliability of PedsQL subscales was determined using Cronbach's Alpha. Values greater than 0.7 were deemed acceptable [16]. Construct validity was assessed using the known groups method using independent sample t-tests to compare PedsQL scores between children with and without vision impairment. Spearman correlations between best-corrected visual acuity and PedsQL™ 4.0 scores were used to further assess construct validity. Intraclass correlations and Bland Altman plots [17] were determined to assess the relationship between child and parent-report scores.

Results

Letters were mailed to parents of 99 potential participants with VI. Of those 73 (74%) agreed to participate in the study. Three were deemed ineligible as their better seeing eye was better than 20/40, for a final sample of 70. All participants were part of a parent-child dyad; 70 included a child with VI and 44 included a child without VI. No parent informants were visually impaired. The mean age was 13 ± 3 years for participants

in both the VI group and the normally sighted group). Participants were mostly white (69% VI, 73% normally sighted) or African American (24% VI, 23% normally sighted).

Table 1: Demographics and Clinical Characteristics:

	Vision Impairment (n=70)	Normal Vision (n=44)	p-value
Age [mean, (SD)]	13.0 (3.1)	12.8 (2.9)	0.8
Gender [n, (% male)]	46 (65.7)	21 (47.7)	0.1
Race [n, (%)]			
White	48 (68.6)	32 (72.7)	0.8
Black	17 (24.3)	10 (22.7)	
Other	5 (7.1)	2 (4.6)	
Premature Birth [n, (%)]	11 (15.7)	5 (11.4)	0.5
Receives special services at school [n, (%)]	35 (50.0)	0 (0.0)	<0.001*
Screening Intelligence Total Standard Score [mean, (SD)]	105.2 (16.3)	106.2 (12.8)	0.7
School Setting [n, (%)]			
Public	45 (64.3)	32 (72.7)	0.02*
Private	10 (14.3)	4 (9.1)	
Homeschool	5 (7.1)	8 (18.2)	
School for the Blind	10 (14.3)	0 (0.0)	
Repeated a grade [n, (%)]	7 (10.0)	3 (7.0)	0.6
Ocular Diagnosis [n, (%)]			<0.001*
Achromatopsia or Cone dystrophy	9 (12.9)	0	
Congenital glaucoma	1 (1.4)	0	
Congenital nystagmus	2 (2.9)	0	
Ocular or Oculocutaneous Albinism	30 (42.9)	0	
Optic Atrophy	8 (11.4)	0	
Optic nerve hypoplasia	4 (5.7)	0	
Other	4 (5.7)	0	
Retinal Degeneration	9 (12.9)	0	
Retinopathy of Prematurity	2 (2.9)	0	
Stargardt macular degeneration	1 (1.4)	0	
None (control)	0 (0.0)	44 (100.0)	
LogMAR Visual Acuity [mean, (SD)]			
Better eye	0.7 (0.2)	-0.1 (0.05)	<0.001*
Worse eye	0.8 (0.3)	-0.06 (0.04)	<0.001*
Binocular	0.7 (0.2)	-0.13 (0.04)	<0.001*
Gender of Parent informant [n, (% female)]	55 (78.6)	36 (81.8)	0.9
Two or more adults in household [n, (%)]	60 (85.7)	40 (90.9)	0.4

*Denotes significance at $p<0.05$

Most parent informants were female (79% VI vs. 82% normally sighted). Demographic characteristics are summarized in Table 1. Best-corrected visual acuity on average was better than 20/20 (-0.1 logMAR) in the children with normal sight. Children with VI had vision ranging from 20/40 (0.3 logMAR) to 20/500 (1.4 logMAR) with a mean visual acuity of 20/100 (0.7 logMAR). Children with VI were no more likely to have been born prematurely or to have repeated a grade, however they were much more likely to receive special services at school (50% VI vs. 0% normally sighted). Standard scores on the Slosson Intelligence Test was not different between children with and without VI.

Quality of Life

The PedsQL™ 4.0 scores can be found in Table 2. All participants and their parent informant completed the survey. The mean scores of 8 to 12-year-old children ranged from 68 (Emotional Health Functioning) to 84 (Physical Functioning) while their parents scored between 69 (School Functioning) and 88 (Physical Functioning). For the teen group, their scores ranged from 80 (Emotional Health Functioning) to 87 (Physical Functioning). Parents of teens' scores ranged from 68 (School Functioning) to 80 (Physical Functioning). Differences between parent and child report can be seen in the Bland-Altman plots in Figure 1. Note that all Scale and Summary Scores show a positive bias, indicating that children perceived their QoL to be better than their parents perceived it to be. In fact, parent and child reports showed only weak to modest correlations (Intraclass Correlation range 0.10 to 0.45 for children 8 to 12 and 0.13 to 0.34 for teens 13 to 18).

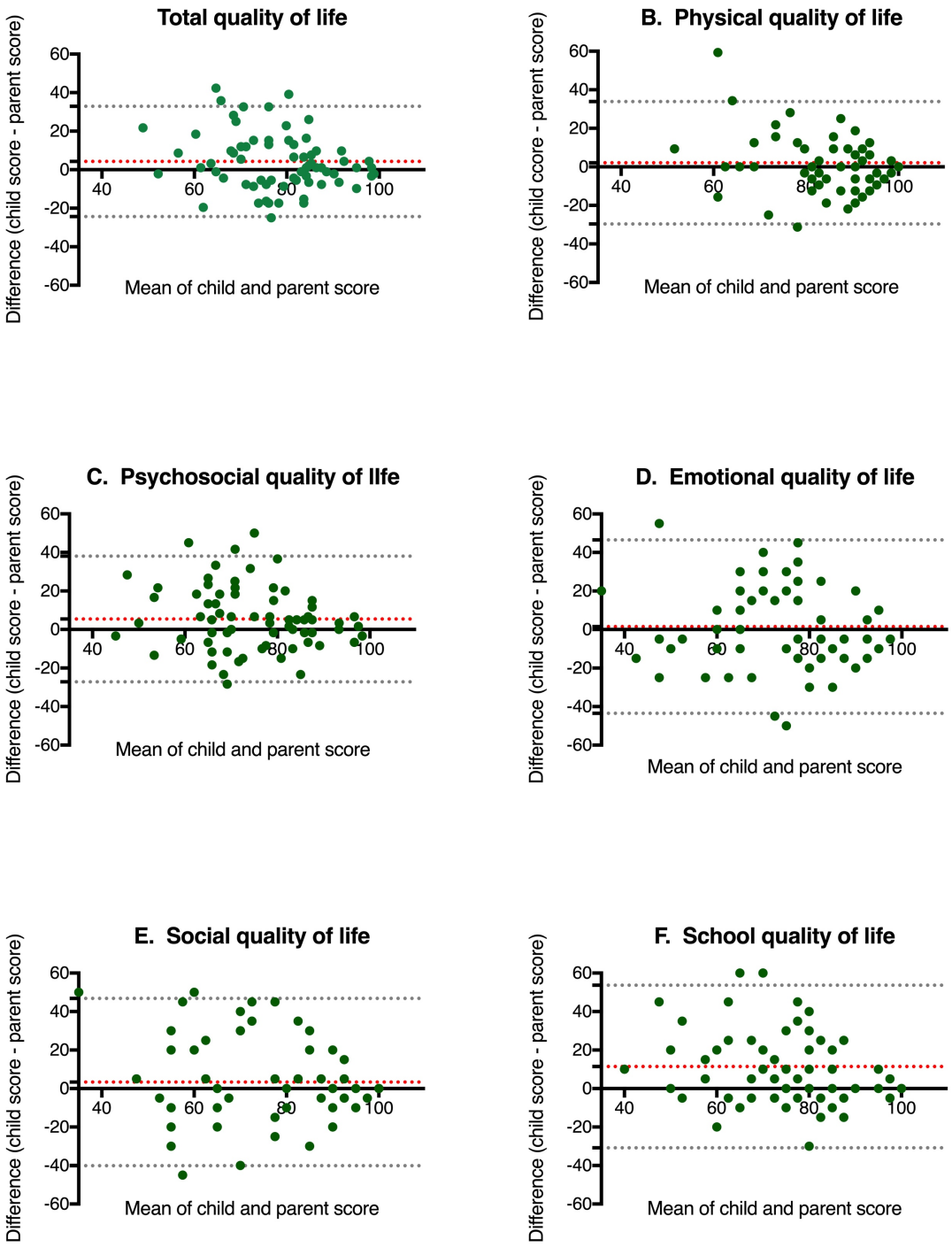

Figure 1: Difference versus means (Bland Altmann) plots comparing child self-report and parent report forms for the PedsQL 4.0

Table 2: Descriptive Statistics for PEDs QL 4.0 from children with Vision Impairment (n=70) and their parents (n=70).

		Mean	Standard Deviation	Median	Score Range	% Ceiling	Cronbach's Alpha
Psychosocial Health Summary Score	Child 8 - 12	73.0	13.7	73.3	46.7 - 100	3.1	0.88
	Parent 8-12	71.8	14.7	73.3	43.3 - 100	3.1	0.88
	Teen 13-18	81.1	12.8	83.3	43.3 - 100	2.6	0.91
	Parent 13-18	72.1	17.6	74.2	33.3 - 100	5.3	0.91
Emotional Health Functioning Scale	Child 8 - 12	67.7	17.2	70.0	35.0 - 100	3.1	0.89
	Parent 8-12	74.2	17.3	70.0	50.0 - 100	15.6	0.90
	Teen 13-18	79.7	18.1	85.0	35.0 - 100	13.2	0.91
	Parent 13-18	71.4	20.6	70.0	20.0 - 100	10.5	0.91
Social Functioning Scale	Child 8 - 12	72.5	22.1	75.0	20.0 - 100	12.5	0.89
	Parent 8-12	72.0	21.4	72.5	10.0 - 100	12.5	0.89
	Teen 13-18	82.4	15.2	87.5	50.0 - 100	18.4	0.91
	Parent 13-18	76.6	21.1	82.5	35.0 - 100	26.3	0.91
School Functioning Scale	Child 8 - 12	78.9	16.1	80.0	50.0 - 100	18.8	0.90
	Parent 8-12	69.2	19.1	70.0	20.0 - 100	6.3	0.90
	Teen 13-18	81.3	14.2	80.0	45.0 - 100	18.4	0.92
	Parent 13-18	68.4	20.3	70.0	25.0 - 100	7.9	0.91
Physical Health Summary Score	Child 8 - 12	84.4	10.9	84.4	53.1 - 100	6.3	0.89
	Parent 8-12	87.8	12.0	89.1	62.5 - 100	28.1	0.90
	Teen 13-18	87.0	12.6	90.6	56.2 - 100	18.4	0.92
	Parent 13-18	80.2	19.1	84.4	28.1 - 100	13.2	0.91
Total Scale Score	Child 8 - 12	77.0	11.7	75.5	52.2 - 100	3.1	0.88
	Parent 8-12	77.4	12.2	79.3	51.1 - 100	3.1	0.88
	Teen 13-18	83.2	11.2	85.9	51.1 - 100	2.6	0.90
	Parent 13-18	75.0	16.5	77.7	38.0 - 100	5.3	0.90

Internal Consistency Reliability

The PedsQL™ 4.0 subscales did not show any floor effects in this population, however some scales did have ceiling effects of up to 28% in for parent report and 19% for child report (Table 2). Cronbach's Alpha was excellent (≥ 0.88) for all subscales for both parent and child forms (Table 2).

Construct Validity: Convergent Validity

Most PedsQL™4.0 subscale scores were moderately negatively correlated with logMAR visual acuity (Table 3). The correlation is negative as higher logMAR scores represent poorer visual acuity and higher PedsQL™4.0 scores represent better QoL. Weaker correlations were found for the teen self-report emotional health functioning scale and school functioning scale as well as for the parent report for 8-12-year-old children on the emotional health functioning scale and physical health summary score. For child, teen and parent report, the Total Score was significantly correlated with acuity ($p<0.05$). This suggests that lower acuity is associated with poorer QoL.

Table 3: Correlations between habitual binocular visual acuity and PedsQL 4.0 Scores

	Form	Child Report	Parent Report
Psychosocial Health Summary Score	Children 8-12	- 0.36	- 0.33
	Teen 13-18	- 0.20	- 0.46
Emotional Health Functioning Scale	Children 8-12	- 0.27	- 0.15
	Teen 13-18	- 0.11	- 0.40
Social Functioning Scale	Children 8-12	- 0.32	- 0.41
	Teen 13-18	- 0.30	- 0.46
School Functioning Scale	Children 8-12	- 0.31	- 0.30
	Teen 13-18	- 0.18	- 0.40
Physical Health Summary Score	Children 8-12	- 0.23	- 0.15
	Teen 13-18	- 0.22	- 0.32
Total Scale Score	Children 8-12	- 0.34	- 0.32
	Teen 13-18	- 0.25	- 0.45

Table 4. Comparison of quality of life between children with and without vision impairment

Domain	Children (8-12) Visually impaired mean ± SD	Children (8-12) Control mean ± SD	*p* value[a]	Teens (13-18) Visually impaired mean ± SD	Teens (13-18) Control mean ± SD	*p* value[a]
Child Report	n = 32	n = 19		n = 38	n = 25	
Physical Functioning	84.4 ± 10.9	88.5 ± 8.7	0.2	87.0 ± 12.6	94.4 ± 5.7	0.003
Emotional Functioning	67.7 ± 17.2	77.4 ± 20.5	0.1	79.7 ± 18.1	86.4 ± 14.6	0.13
Social Functioning	72.5 ± 22.1	84.2 ± 22.3	0.1	82.4 ± 15.2	91.8 ± 15.9	0.02
School Functioning	78.9 ± 16.1	88.4 ± 13.5	0.04	81.3 ± 14.2	88.8 ± 12.5	0.04
Total Score	77.0 ± 11.7	85.1 ± 11.6	0.02	83.2 ± 11.2	90.9 ± 8.4	0.005
Parent Report	n = 32	n = 19		n = 38	n = 25	
Physical Functioning	87.8 ± 12.0	92.1 ± 15.9	0.3	80.3 ± 19.1	94.3 ± 8.0	0.0002
Emotional Functioning	74.2 ± 17.3	82.4 ± 16.8	0.11	71.4 ± 20.6	91.0 ± 10.9	<0.001
Social Functioning	72.0 ± 21.4	92.6 ± 11.5	<0.001	76.6 ± 21.1	94.2 ± 9.1	<0.001
School Functioning	69.2 ± 19.1	86.1 ± 21.1	0.005	68.4 ± 20.3	87.6 ± 14.9	<0.001
Total Score	77.4 ± 12.2	88.8 ± 12.2	0.002	75.0 ± 16.5	92.1 ± 6.5	<0.001

[a] *P* value of < 0.05 was considered statistically significant.

Construct Validity: Discriminative Validity

For children, scores were significantly different between those with and without VI for the School Functioning Scale (p=0.04) and Total Score (p=0.02) (Table 4). For teens, significant differences were found for Physical Functioning (p=0.003), Social Functioning (p=0.02), School Functioning (p=0.04) and Total Score (p=0.005). Parent report for children 8 to 12 was significantly lower for those with VI compared to those without VI for Social Functioning, School Functioning and Total Score. Parent report for Teens (13-18) was significantly lower across all scales for those with VI versus those without VI.

Discussion

The PedsQL^{TM}4.0 was evaluated to determine the internal consistency reliability and construct validity of the instrument in children and teens with VI to determine if this instrument should be used in this population. We sought to determine if this generic health-related QoL instrument would detect differences between children with and without VI and within the group with VI if worse VA would be associated with lower QoL scores. Overall, the use of the PedsQL^{TM}4.0 in children with VI was supported. Our sample included children without other co-morbidities and with vision better than 20/800. However, the mean binocular acuity was 0.7 logMAR (20/100). Despite relatively good central acuity, and mostly stable, congenital conditions (for example: albinism, achromatopsia), the PedsQL^{TM}4.0 did discriminate between groups of children with and without VI and lower scores were associated with worse visual acuity.

A small study (n= 38) in the United Kingdom used the PedsQL^{TM}4.0 to assess QoL in children with inherited retinal conditions found even lower QoL than in our study [18] (Total score 65.5 ±16.7, Physical Health Score 65.1 ±20.3 and Psychosocial Health Score 65.7 ±16.4 for Child report and Total score 60.6 ±17.9, Physical Health Score 59.4 ±21.6 and Psychosocial Health Score 62.0 ±17.0). However, they mailed surveys to families who consented to participate, and only 29% of those contacted participated. Therefore, it may have only been those with the poorest QoL that elected to complete the surveys. Additionally, it cannot be guaranteed that the child completed their survey on their own. Many of the conditions may have been progressive forms of retinal degenerations (exact diagnoses were not provided) and the fear of the future in children with a progressive disease may have contributed to lower scores as well.

Interestingly, teens in our sample scored higher on most scales and summary scores than younger children, however parents of both groups scored their children approximately the same. In a study of children with glaucoma, teens also reported better QoL than younger children with the same diagnosis [19]. Similar findings were reported in a small study on microphthalmia [20]. This may indicate that as children mature they learn to cope with their VI better so that it has less impact on their QoL. It is unclear why the same would not be found for parent proxy report. One possible explanation is that problems related to the child's VI led the parent to seek low vision rehabilitation, emphasizing the impairment for the parent; while the child received accommodations and adaptive equipment which likely de-emphasized the impairment for the child.

Problems with proxy reporting for pediatric QoL have been well documented. In one large meta-analysis (119 studies), the correlation between child and proxy was only

0.22 [21]. Reasons for differences between parent and child report include the informant's own biases and personal problems, denial, provision of answers deemed acceptable by the informant and simply lack of knowledge [22]. Additionally, in our study many of the children had conditions that were hereditary and parents may have felt responsible for their child's impairment which could also affect their survey answers. Parent proxy reports had only weak to moderate correlations with child report, with children reporting somewhat better QoL. Examination of the Bland Altman plots in Figure 1 show that at times the discrepancy between child and parent report is quite large across all domains. The PedsQL^{TM}4.0 was chosen for use in this current study as it covered the topics most frequently discussed by both parents and children in our focus group study. In that study, children were most concerned with psychosocial aspects of their VI while parents were most concerned about school functioning [13]. The difference in scores on the PedsQL^{TM}4.0 between parents and children further supports its use in this population as differences were expected *a priori* based on the focus group results.

Strengths of this study include measurement of both parent and child report, independent of one another but on the same day. Additionally, children in our sample had normal intelligence and no significant comorbid conditions, enabling assessment of the impact of VI rather than the impact of multiple disabilities on QoL. Selection bias was possible as all participants were recruited from a single low vision service in a department of ophthalmology. Parents who take their children for clinical low vision evaluations may be more concerned about the impact of their child's VI on their daily life and their future. It could also be true that those children with poorer QoL are those most likely to need and receive a low vision evaluation. This may lead to lower scores.

However, the converse may be true in that the child would be more likely to have the tools and accommodations needed to compensate for their VI in school and elsewhere leading to higher scores.

Conclusion

The PedsQL™ 4.0 is a valid, well-established QoL instrument for use in children. It is a reliable measure for children with VI and can discriminate between groups of children with and without VI. This study demonstrates the considerable impact that VI has on daily life in children and that the impact is related to the severity of VI.

Acknowledgement

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CHAPTER 4

ACCOMMODATIVE RESPONSE IN CHILDREN WITH LOW VISION

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Introduction

Children with irreversible vision impairment (VI) tend to hold reading materials much closer than other children (the object's image on the retina is larger when it is held closer) as a primary means to compensate for their vision impairment. Thus, if holding objects closer is a rehabilitation strategy for reading that is encouraged for visually impaired children, it is important that they have adequate accommodative ability to maintain focus at that distance. If there is anomalous accommodation, then remediation with lenses and/or vision therapy can be part of the rehabilitation strategy.

Accommodation is the process whereby the natural intraocular lens changes shape to produce the appropriate refractive power to keep images clear on the retina. Reading at closer distances requires more accommodative effort than reading at longer distances. The accommodative demand in diopters (D) is the reciprocal of the test distance in meters(m); 4D of accommodation is required at 0.25m whereas 20D is needed at 0.05m. The accuracy of accommodation is known as the accommodative response and is determined by subtracting the actual accommodation produced from the accommodative demand with positive values indicating a "lag" of accommodation and negative values indicating a "lead" of accommodation.

Experts agree that blur is a stimulus to accommodation[1-4]. Many additional factors are known to affect accommodative response including vergence, proximity and chromatic aberration.[4] Depth of Focus refers to the distance both in front and behind the retina where the image is deemed to be in focus by the observer. Factors that contribute to depth of focus, such as target contrast[5], spatial frequency[6], luminance[7]

and pupil diameter[8] can vary significantly before there is any effect on accommodation. However, according to Ciuffreda[9] the accommodative system is much more sensitive to the effects of target retinal eccentricity[10] and retinal-image motion[11]. The latter two are likely to degrade accommodation in VI due to central scotomas and/or nystagmus in addition to the effects of the acuity impairment.

The purpose of this study is to characterize the accommodative response of children with VI and compare it to children with normal vision. Additionally, we will determine test-retest reliability for Nott dynamic retinoscopy and autorefractometry. We will determine the correlation between dynamic retinoscopy and autorefractometry as dynamic retinoscopy is a clinical test that does not require specialized equipment. The utility of this information is that it may help us to understand the near symptoms of children with VI who frequently complain of visual fatigue[12] as well as to design appropriate rehabilitation strategies.

Methods

This study was approved by the University of Alabama at Birmingham Institutional Review Board for Human Use and adhered to the tenets of the Declaration of Helsinki. A parent or guardian provided written informed consent. Children aged 14 and older also provided written informed consent, whereas younger children provided written assent.

Participants with VI were recruited from the patient base of one of the authors (DKD). Participants with normal vision were recruited using flyers in the clinic waiting

room. Eligibility for participants with VI included having VI of organic etiology, clear media and a natural intraocular lens. Eligibility for children with normal vision included best-corrected visual acuity in each eye of 0.1 logMAR (20/25) or better, at least 50 seconds of stereopsis and refractive error between +4D and -4D with no more than 1.5D astigmatism or 0.75D anisometropia. For both groups, participants were excluded from data analysis if their cycloplegic refractive error differed by ±4D or more than their manifest refraction. Information about demographics and ocular health were collected from the parent and from the medical record. Ocular health status was confirmed by dilated examination. The Slosson Intelligence Test-revised 3rd edition[13] was administered to all participants at the first visit. Participants had their visual acuity measured with best correction in place using the EVA Tester (Jaeb Center, Tampa, FL) binocularly and then monocularly at a 3-meter test distance using the eETDRS protocol.[14] EVA scores were converted to logMAR using the formula: 1.7 – (0.02)(letter score). Refraction was determined using retinoscopy and/or loose lenses as appropriate for the child. Near reading acuity was measured using the MNREAD chart (Precision Vision Inc, LaSalle, IL) at 20cm. Ocular alignment was measured using the cover test at 20cm and 3 meters, Worth 4-dot test and Random Dot 2 Stereoacuity Test (Vision Assessment Corporation, Elk Grove Village, IL).

After all accommodative testing was completed at the first visit only, each patient was cyclopleged using 2 drops of 1% cyclopentolate in each eye, with the instillation of the 2nd drop 5 minutes after the first. Cycloplegic autorefraction was measured using the WAM 5500 while fixating a target located 8.5 meters away 30 to 45 minutes later.

All participants wore their habitual correction for testing unless their manifest refraction differed by ≥ 1D spherical equivalent, in which case they wore the manifest refraction in a trial frame. Participants wearing bifocals also had their accommodative response measured in a trial frame. The target was an Ulster-Cardiff Accommodation Cube (UC-Cube), which is an internally illuminated 4.4 x 4.4 x 4.4-centimeter white cube with high contrast black targets. The cube was illuminated for all participants except those with achromatopsia who found it too bright. Room lighting was dim for all participants. The standard cube with fish targets were used as the fish were of varying sizes and had details that could be discussed with the child to ensure attention to the target (Figure 1). An adapter was made for the WAM 5500 to mount the UC cube and ruler to the WAM 5500 (Figure 2). For dynamic retinoscopy, the standard, unmodified

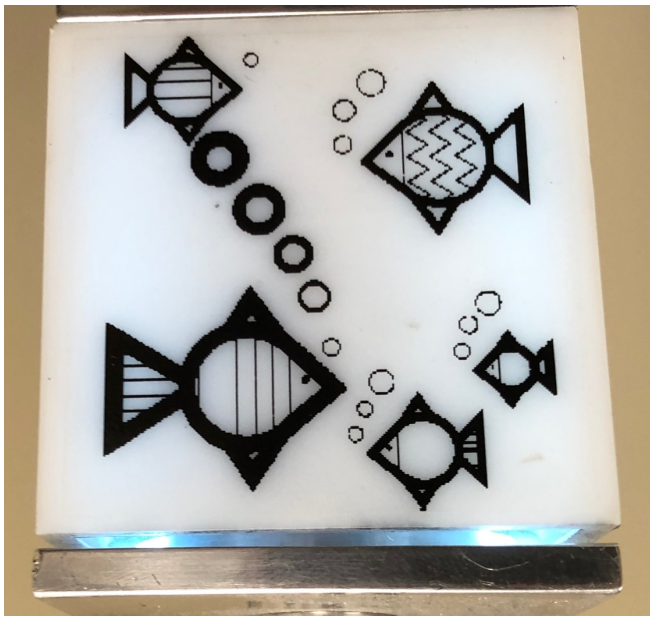

Figure 1: Accommodative stimulus target

UC Cube and ruler was used. Two test distances were assessed: 16.6 cm and 25cm, corresponding to accommodative demands of 6D and 4D, respectively. The eye with better acuity was measured. If acuity was equal, the dominant eye was measured. Ocular dominance was determined by having the participant fixate the examiners right eye through an aperture held in both hands at arm's length. The fixating eye was deemed dominant. All accommodative response testing was performed with both eyes open as occlusion tends to increase nystagmus in people with nystagmus. It has been shown that the order of target presentation does not significantly affect the results [15], therefore the targets were presented in order of increasing accommodative demand. Participants were randomized to having Nott dynamic retinoscopy or autorefractometry done first. Retesting occurred using the same procedures no less than 1 week and no more than 3 weeks later.

Figure 2: Grand Seiko WAM 5500 with UC-Cube mounted to instrument

Autorefractometry:

The WAM 5500 (Grand Seiko, Japan) is an open-field autorefractor that measures monocular refractive state while fixating targets binocularly. For this study, the WAM 5500 was connected to a laptop computer with the included WCS-1 Hi Speed Mode Control software, and data were collected dynamically at 5Hz. In the dynamic mode, the WAM 5500 determines the spherical equivalent refraction (sphere + ½ cylinder power) and pupil diameter. This data along with the eye measured and a time stamp is stored in a Microsoft Excel file.

Participants were seated comfortably at the WAM 5500 with their head and chin in the appropriate rests on the instrument. The UC-Cube was positioned 25cm from the eye. The participant was asked to focus on the picture and keep it clear, and was engaged in discussion about the pictures on the cube to help ensure appropriate effort. Data were collected for up to 2 minutes, with the goal of obtaining at least 20 seconds of recording with the instrument aligned with the pupil. After a 2-minute rest period during which the participant was instructed to look in the distance, the procedure was repeated. The same procedure, including the rest period was then repeated twice for the 16.67cm test distance (6D demand). In the dynamic mode, measurements are not seen by the examiner. Missing data can only be detected once the Excel spreadsheet is reviewed, so when in doubt, the examiner erred on the side of collecting more data than was needed. The sign of the spherical equivalent refraction measurement was changed (plus to minus and vice versa) and was subtracted from the accommodative demand to yield the accommodative response. Measurements were discarded if they were not deemed to be physiologically possible: a) the difference between successive measurements was > 10D per second (limit

of the human accommodation system)[16] or b) the accommodative response was outside the range of -8D to +8D for the 4D demand condition and -8D to +10D for the 6D demand condition to allow for significant lead/lags as well as uncorrected or under-corrected refractive error up to the maximum ±4D permitted.

Nott Dynamic Retinoscopy:

The UC-cube was set initially to 25 cm and the participant was engaged in conversation about the picture. The examiner oriented the streak vertically and began examining the reflex at 50cm. At this distance, "against" motion was seen and the retinoscope was moved closer until neutrality was achieved; the examiner continued to move the retinoscope until "with" motion was seen and then bracketed the response to identify the final point of neutrality. A second examiner recorded the distance. Testing was then performed in the same manner for the 16.7cm target distance. Both distances were then repeated. Accommodative response was determined by subtracting the reciprocal of the distance of the point of neutrality from the eye in meters from the accommodative demand.

Data analysis:

Data analysis was conducted using SAS 9.0 (SAS (version 9.4 SAS, Cary, NC) or Prism 8 for Mac (GraphPad Software, San Diego, CA). Demographic and clinical data was summarized using descriptive statistics and Chi Square or Paired Wilcoxon Sign Rank test Test as appropriate. Residual refractive error for autorefractometry was determined by subtracting the spherical equivalent (Sphere + 1/2cylinder power) of the refractive correction used for testing from the spherical equivalent for the cycloplegic autorefraction. Residual refractive error for dynamic retinoscopy was determined by

subtracting the refractive power in the horizontal meridian of the refractive correction used for testing from the refractive power in the horizontal meridian for the cycloplegic autorefraction since all testing was conducted with the retinoscope streak oriented vertically. Power in the horizontal meridian was calculated using the power vector method.[17] Data from the dynamic mode for the WAM was summarized as mean, standard deviation, minimum and maximum for each test condition for children with VI and with normal vision. Test-retest reliability was assessed with intraclass correlation coefficients (Shrout-Fleiss reliability, random set) of the accommodative response for each demand level at each visit and trial separately for normal participants and those with VI. The relationship between WAM near autorefractometry and Nott retinoscopy was also assessed using Intraclass correlations. Data from all 4 measurements (2 trials per visit X 2 visits) were then pooled to provide a single measure for each technique and demand level. Factors that might contribute to reduced accommodation were investigated using either correlations, Kruskal Wallis test or a Chi-square test, as appropriate. The 95% range for normal accommodation was calculated as the mean for the control group ±1.96 x standard deviation for each test and demand. Statistical significance was set at $\propto$=0.05 (two-tailed) for all analyses.

Results

Letters were sent to parents of 99 children with VI in grades 1 through 12 who did not have a history of developmental delay or cognitive impairment in the medical record. Of those, 77 agreed to participate and 74 were eligible for the study. Three had visual acuity in their better eye greater than 20/40 and were excluded. An additional 12

Table 1: Demographic and Ocular Characteristics of Participants

Characteristic	Participants with Vision Impairment (N=62)	Participants with Normal Vision (N=45)	p-value
Age (mean ± SD)	12.5 ± 3.4 years	12.7 ± 3.1 years	0.8
Gender (n, %)			
Female	21 (34%)	23 (51%)	=0.07
Male	41 (66%)	22 (49%)	
Race (n, %)			
White	44 (71%)	33 (73%)	=0.7
Other	18 (29%)	12 (27%)	
Premature Birth (n, %)	7 (11%)	5 (11%)	=1.0
Screening Intelligence Total Standard Score (mean ± SD)	107 ± 14	107 ± 13	=0.9
Ocular Health Diagnosis (n, %)			
Achromatopsia or Cone dystrophy	9 (14.5%)		
Congenital nystagmus	2 (3.2%)		
Ocular or Oculocutaneous Albinism	26 (42%)		
Optic Atrophy	8 (12.9%)		<0.001
Optic nerve hypoplasia	4 (6.5%)		
Other	5(8.1%)		
Retinal Degeneration	8 (12.9%)		
None	0	45 (100%)	
Ever diagnosed with ADHD (n,%)	13 (21%)	11 (24%)	=0.7
Medicated for ADHD (n,%)	9 (69%)	5 (45%)	=0.2
Eyes feel tired when reading or doing close work (n,%)			
Never	10 (16%)	22 (49%)	
Infrequently/not often	17 (27%)	13 (29%)	<0.0001
Sometimes	22 (35%)	10 (22%)	
Fairly often	9 (15%)	0	
Always	4 (6%)	0	
Words blur or come in and out of focus when reading or doing close work (n, %)			
Never	26 (42%)	34 (77%)	
Infrequently/not often	13 (21%)	4 (9%)	=0.002
Sometimes	16 (26%)	6 (14%)	
Fairly often	4 (6%)	0	
Always	3 (5%)	0	
Visual Acuity (logMAR) (mean, SD)			
Tested eye	0.68 ±0.22	-0.09 ±0.05	
Fellow eye	0.76 ±0.23	-0.08 ±0.05	
Binocular	0.65 ±0.22	-0.13 ±0.05	<0.0001
MNREAD minimum print size OU (logMAR) (mean, SD)	0.57 ±0.3	-0.15 ±0.1	<0.0001
Nystagmus (n, %)	42 (69%)	0	<0.0001
Fusion on Worth 4-dot (n, %)	34 (55%)	45 (100%)	<0.0001
Stereopsis ≥100 sec arc (n,%)	18 (29%)	45 (100%)	<0.0001

participants with VI were excluded from analysis as both their manifest refraction and their habitual correction differed from their cycloplegic autorefraction by more than ± 4D. All children with normal vision recruited for the study were eligible for participation. The final sample included 62 children with VI and 45 children with normal vision.

Participants with and without VI were similar with respect to age, race, intelligence, diagnosis of ADHD and premature birth (Table 1). There were more males than females among the participants with VI but not among participants with normal vision. Common diagnoses associated with VI were albinism, achromatopsia or cone dystrophy and optic atrophy. Children with VI had more complaints about their eyes feeling tired when doing near work (18% reported fairly often or always versus 0% for children with normal vision, $p<0.0001$). Children with VI were also more likely to report words blurring or coming in and out of focus when reading or doing close work (37% reported this occurred at least sometimes versus only 14% of their normally sighted peers, $p=0.0006$).

Mean binocular visual acuity at distance for participants with VI was 0.65 ± 0.22 logMAR (20/90) versus -0.13 ± 0.05 logMAR (20/15) for participants with normal vision. Near reading acuity was also significantly better for participants with normal sight (Table 1). Over two-thirds of participants with VI had nystagmus and 53% had strabismus whereas no participants with normal vision had either. Twenty percent of participants with normal vision wore glasses versus 66% of children with VI. Many in both groups had uncorrected or under-corrected refractive error both with regards to spherical equivalent that is measured by the autorefractometer and power in the

horizontal meridian that is measured by dynamic retinoscopy with the streak vertical (Figure 3). The refractive correction for testing was significantly different from the cycloplegic autorefraction for both spherical equivalent refractive error and J0 refractive error (horizontal meridian) for children with and without VI ($p<0.001$). In many cases hyperopia was under-corrected while myopia was over-corrected leading to a need for increased accommodation at near. This, however, did not impact accommodative accuracy as measured by near autorefraction or Nott dynamic retinoscopy.

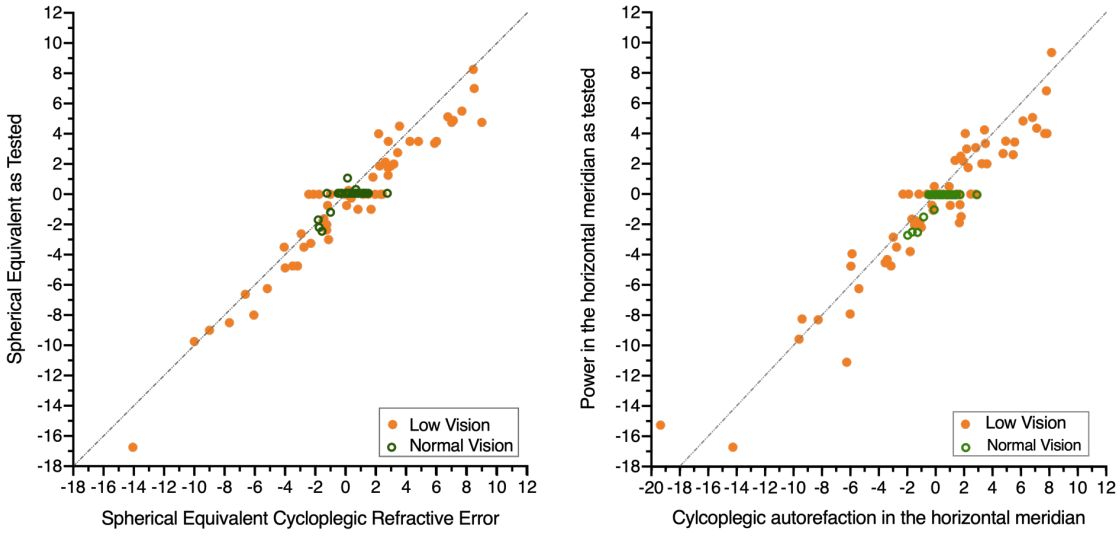

Figure 3: Comparison of spherical equivalent correction for testing versus spherical equivalent cycloplegic refractive error.

Results from each trial and each demand level by test and vision status are presented in Table 2. Test-retest reliability for the WAM 5500 was excellent within visits and between visits for both children with and without VI. Nott retinoscopy had somewhat lower test-retest reliability (Table 3). Correlations between the 2 tests were moderate for children with VI at both demands and for children with normal vision at the 6D demand, however correlations were weak for the 4D demand primarily at the first

visit. (Table 4). Difference versus means plots show that as the lag of accommodation increases, so does the difference in results between the tests (Figure 4).

Table 2: Descriptive statistics for accommodative response by test and vision status

Test	Group	Visit	Trial	n	Median	IQR	Min	Max
Near Autorefraction 4 diopter Demand	Normal Vision	1	1	45	1.02	0.83 – 1.25	0.10	3.32
			2	45	1.01	0.19 – 2.79	0.19	2.79
		2	1	45	0.95	0.76 – 1.22	0.29	1.63
			2	45	0.93	0.39 – 1.94	0.39	1.94
	Vision Impairment	1	1	61	1.81	1.01 – 2.55	0.00	4.45
			2	62	1.71	1.03 – 2.29	-0.24	4.34
		2	1	60	1.64	1.05 – 2.07	-2.31	5.29
			2	61	1.62	1.01 – 2.22	-1.77	4.36
Near Autorefraction 6 diopter Demand	Normal Vision	1	1	45	1.29	1.03 -1.53	0.19	3.23
			2	45	1.25	1.09 – 1.57	-0.04	2.60
		2	1	45	1.19	0.77 – 1.50	0.11	2.45
			2	45	1.22	0.79 – 1.60	-0.28	2.10
	Vision Impairment	1	1	62	2.39	1.61 – 3.43	0.04	6.79
			2	62	2.35	1.76-3.35	0.46	6.40
		2	1	61	2.20	1.67 – 3.11	0.18	6.02
			2	61	2.21	1.51 – 2.93	0.49	5.60
Nott Dynamic Retinoscopy 4 diopter Demand	Normal Vision	1	1	45	0.43	0.30 – 0.67	-0.26	1.18
			2	45	0.30	0.15 – 0.67	-0.35	1.37
		2	1	45	0.43	0.23 – 0.67	-0.17	1.22
			2	45	0.36	0.15 – 0.55	-0.17	1.14
	Vision Impairment	1	1	62	0.90	0.55 – 1.47	0.00	2.89
			2	62	0.88	0.49 – 1.37	0.08	2.97
		2	1	62	0.97	0.55 – 1.30	-0.26	2.63
			2	62	0.92	0.61 – 1.26	-0.35	2.28
Nott Dynamic Retinoscopy 6 diopter Demand	Normal Vision	1	1	45	0.74	0.29 – 1.00	-0.25	2.77
			2	45	0.74	0.29 – 0.87	-0.90	2.88
		2	1	45	0.44	0.29 – 0.74	-0.45	1.45
			2	45	0.44	0.12 -0.74	-0.67	1.45
	Vision Impairment	1	1	62	1.70	1.12 – 2.43	-0.25	3.87
			2	62	1.79	1.12 -2.55	-0.45	3.73
		2	1	62	1.51	1.00 – 2.30	-0.67	3.67
			2	62	1.51	1.00 – 2.30	-0.06	3.65

IQR = interquartile range Min = minimum Max = maximum

Table 3: Intraclass Correlations for Accommodative Response measured by near autorefraction or Nott dynamic retinoscopy by Accommodative Demand and Vision Status

Test	Vision Status	Demand	Between Trials		Between Visits	
			Visit 1	Visit 2	Trial 1	Trial 2
Near Auto-refraction	Vision Impairment	4D	0.82	0.91	0.69	0.78
		6D	0.94	0.94	0.81	0.79
	Normal Vision	4D	0.93	0.91	0.72	0.79
		6D	0.92	0.93	0.85	0.88
Nott Retinoscopy	Vision Impairment	4D	0.76	0.88	0.61	0.60
		6D	0.87	0.92	0.53	0.60
	Normal Vision	4D	0.80	0.57	0.54	0.62
		6D	0.74	0.66	0.21	0.39

Table 4: Correlations between Nott dynamic retinoscopy and near autorefraction between visits and overall.

Vision Status	Accommodative Demand	Visit 1	Visit 2	Overall
Vision Impairment	4D	0.40	0.47	0.44
Vision Impairment	6D	0.40	0.47	0.44
Normal Vision	4D	0.13	0.45	0.13
Normal Vision	6D	0.45	0.22	0.33

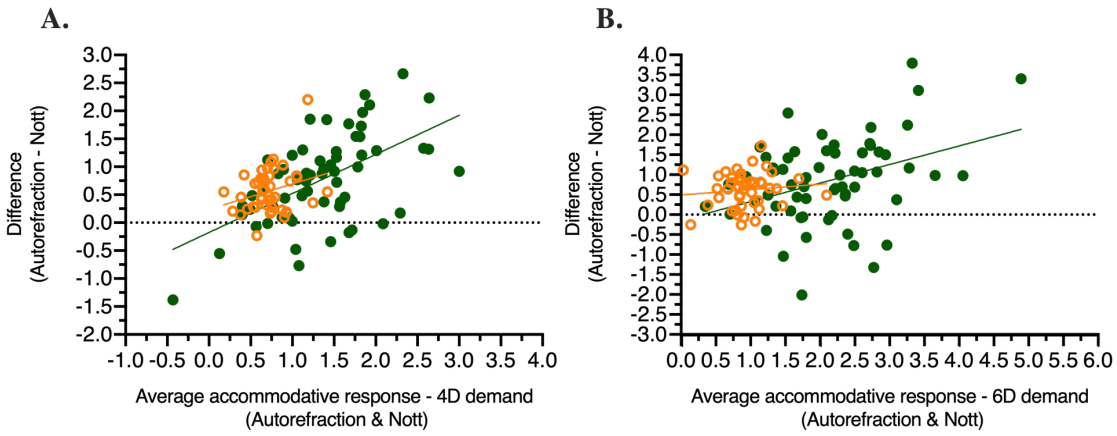

Figure 4: Difference versus means plots for accommodative response over 2 visits at 4D and 6 D demands

Histograms of the pooled accommodative response for each test and demand level are shown in Figure 5. The WAM 5500 tended to measure larger lags of accommodation than Nott dynamic retinoscopy. Greater lags were also seen for the 6D versus 4D demand condition for both tests for both children with VI and normal vision. For the 4D demand condition, 40% (n=25) of participants with VI had lags greater than the 95% range of normal for the normal vision control group by Nott dynamic retinoscopy and 55% (n=34) by near autorefractometry. For the 6D demand, 70% (n=43) exceeded the 95% range of normal for the normal vision control group by Nott dynamic retinoscopy and 61% (n=38) by near autorefractometry.

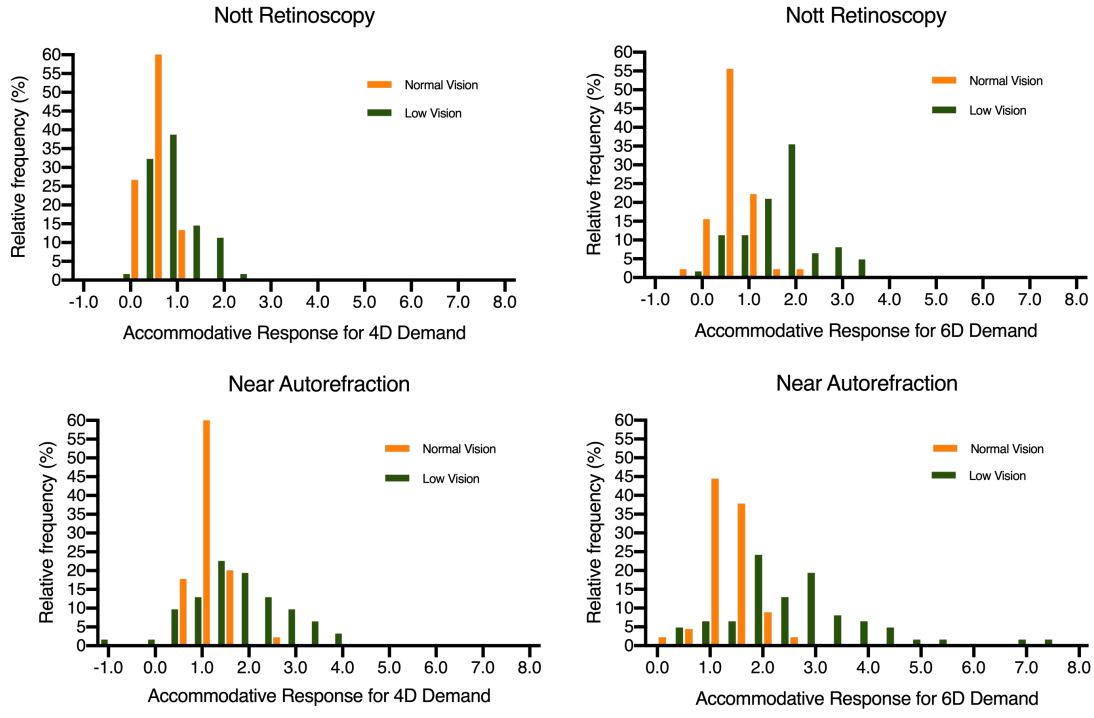

Figure 5: Distribution of accommodative responses (lag or lead) by test and demand.

There was no association between accommodative response (by either test or demand) and refractive error, gender or symptoms of blur or focusing difficulties.

However, poorer binocular acuity was associated with greater lags of accommodation for both the 4D and 6D demand conditions measured by near autorefractometry ($p= 0.009$ for 4D and $p = 0.01$, respectively) but not by Nott dynamic retinoscopy. Those in the VI group without fusion on the Worth 4-dot test, indicating a lack of basic binocular function, were compared to those with fusion and to the group with normal vision. The differences were statistically significant for each test/demand (Kruskal-Wallis test, $p<0.0001$).

Discussion

This work included the largest sample of children with VI to date in a study on accommodative response. It confirms that the majority of children with VI under-accommodate for near targets. This is important, as children with VI are known to use very close working distances for reading and other detailed tasks. They also frequently report symptoms of visual fatigue and eye strain.[12] Here, we have shown that they do not accommodate as well as their normally sighted peers as measured by a common clinical test and by a gold standard autorefraction. Accommodation has been studied in some groups of people with vision impairment. Reduced accommodative response has been shown in small numbers of subjects with albinism[18], juvenile macular degeneration[19], congenital nystagmus[20] and achromatopsia.[21] Reduced accommodative response has also been shown in amblyopia,[6] Down Syndrome[22] and autism spectrum disorder.[23]

Leat and Mohr[24] examined the accommodative response of 21 participants with low vision (aged 3 to 35 years) and found that 85% were outside the 95% range of

normal and that the errors were often more than predicted by the increased depth of focus due to their low vision. Similar to our study, there were no statistical associations with visual acuity, age, presence of nystagmus or refractive error when using Nott dynamic retinoscopy.

McClelland and Saunders [25] using Nott retinoscopy studied 125 school aged children from 4 to 15 years of age and using regression analysis found no difference in accommodative response between age groups, but that the accommodative lag did increase with stimulus demand (0.30 ± 0.39 at 4D and 0.74± 0.58 at 6D). Also using Nott retinoscopy, we found similar results among our participants with normal vision (0.43 ± 0.27 at 4D and 0.58 ± 0.40 at 6D). Participants with low vision had an even greater increase in accommodative lag with increasing stimulus demand (0.99 ±0.54 at 4D and 1.75 ± 0.83 at 6D).

Our near autorefraction results and Nott dynamic retinoscopy were moderately correlated. The accommodative response was less (the lag of accommodation was greater) as measured by the WAM 5500 compared to dynamic retinoscopy. This is consistent with the findings of the COMET-2 study[26] that compared near autorefraction with a Grand Seiko WR-5100K to both Nott and MEM dynamic retinoscopy. They found that neither Nott or MEM had adequate sensitivity and specificity to identify myopic children with an accommodative lag ≥ 1.00D measured by the autorefractor. The mean accommodative lag measured by the WAM 5500 was greater than that of either dynamic retinoscopy test by approximately 0.5D, which is similar to what was found here for children with normal vision. For Nott dynamic retinoscopy, the examiner is observing the response and may encourage active

focusing more when they see an increased lag whereas the encouragement to maintain active focusing would not be biased with the actual measurements of the WAM 5500 since they were not visible. This difference may contribute to smaller lags on dynamic retinoscopy.

Some might argue that accurate accommodation is not necessary in vision impairment owing to the larger tolerance for defocus in people with low vision. Legge et al[27] showed that in 30 adult low vision observers the amount of dioptric blur needed to reduce acuity 0.1 log unit ranges from about 0.5D for those with near normal acuity to up to 5D for those with 20/800 acuity. However, there is significant variability among observers and the majority of those with acuity better than 20/200 had 1D or less tolerance for defocus. Both Legge [28] and Chung [29] have shown in people with normal vision that with increased blur the reading curves are shifted toward larger print size and the critical print size as well as reading acuity suffer. This shift in the reading curve due to blur may preclude a child from accessing print in the classroom who could access it with appropriate correction. Additionally, Chung [29] found that reading speeds were 23% slower when 3 diopters of blur were present. Some of our participants had lags of accommodation of that magnitude or greater. Further research is needed to explore the relationship of accommodation with near visual acuity and reading ability in children with low vision.

Clinical experience suggests that most children with VI use working distances of 10-20cm. A large print (2M or approximately 16-point Arial font) letter at a distance of 10cm has a fundamental spatial frequency of 1.5 cycles per degree. Charman and Tucker [30] found that for spatial frequencies <1 cycle/degree the eye adopts a

response similar of that to the empty-field value, but that as the spatial frequency is increased above 1 cycle/degree the response rapidly becomes more accurate and that at ≥3 cycles/degree the eye attempts to achieve an optimal response. Studies have also shown that the lower spatial frequencies are important in guiding the accommodation response to its final level [30, 31]. Since accommodation is well maintained for square-wave grating stimuli of all spatial frequencies less than 20 cycles per degree, [32] one would expect that for broad-band stimuli such as the pictures we used, accommodation would also be maintained. Therefore, it is reasonable to expect good responses from patients with low vision.

Although the reason for poor accommodative accuracy in children with low vision is not known, there are several possibilities. First, children with VI do hold materials close so that their image subtends a larger angle on the retina. They may find a larger, but blurry image preferable to the extra work required to maintain a clear image. Second, convergence and accommodation are neurologically linked. As many of these participants had reduced or no binocular vision there is less incentive for convergence which may in turn contribute to less accommodation. Our results showing an increased lag of accommodation between the 3 groups when the VI group was divided by fusion on the Worth-4 dot test supports this. Third, children with VI may simply be more tolerant of blur due to an increased depth of focus. This is supported by our finding using near autorefractometry that higher lags were associated with poorer visual acuity at both the 4 and 6D demand levels. However, Ciuffreda's work [6, 33, 34] demonstrated that amblyopic eyes show reduced static accommodative response to broadband stimuli but that the increased depth of focus

generally found in eyes with amblyopia cannot account for most of the accommodative loss.

Strengths of our study include a large population of children with vision impairment whose cycloplegic refractive error was known so that children with large amounts of uncorrected refractive error were excluded. A weakness of this study was that the participants were all recruited from a single low vision rehabilitation clinic and those children who are seen in a low vision service may have more focusing difficulties than those not seeking vision rehabilitation. Additionally, there was only a single examiner performing Nott retinoscopy that examiner was not masked as to the visual status of the participant. Masking would not have been possible in patients with nystagmus which comprised the majority of participants, so masking was not attempted.

In summary, near accommodative responses are less accurate in children with low vision, yet the reason is poorly understood. Accuracy decreases with decreasing stimulus distance. This is particularly problematic in children with VI since they depend upon the shorter viewing distances for magnification. They report significant symptoms of fatigue and blur when reading, yet these complaints do not correlate with accommodative response. This work suggests that both convergence and visual acuity may play a role. Both Nott dynamic retinoscopy and open field near autorefraction are useful in children with VI. However, most clinicians do not have access to an open field autorefractor. They should keep in mind that the actual lag experienced by a low vision patient is likely larger than that measured by a clinical technique.

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CHAPTER 5

REPEATABILITY AND VALIDITY OF THE MNREAD TEST IN CHILDREN WITH VISION IMPAIRMENT

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Format adapted for dissertation

Abstract

Purpose: To evaluate the test-retest reliability and validity of the MNREAD test for use in children with VI and to compare their performance to that of normally sighted children.

Methods: Children with (n=62) and without (n=40) VI were administered the MNREAD test and the Jerry Johns Basic Reading Inventory (BRI) on 2 study visits, 1 to 3 weeks apart. Maximum Reading Speed, Critical Print Size and Reading Acuity were determined for the MNREAD and test-retest reliability was evaluated. Reading rate for the MNREAD test was compared to the BRI results.

Results: Strong correlations between visits were found for all MNREAD parameters (0.68 to 0.99). Older, but not younger, children with VI read significantly slower on both the MNREAD and the BRI than children with normal vision ($P < 0.05$). Reading rates between the two tests were strongly correlated ($r=0.88$). Reading rate increased 4.4 wpm/year (VI) and 10.6 wpm/year (normal vision) on the MNREAD test. It increased by 5.9 wpm/year (VI) and 9.7 wpm/year (normal vision) on the BRI. Poorer visual acuity was associated with slower reading rates on the MNREAD, but not the BRI, as the MNREAD relies largely on visual factors and the BRI also relies on linguistic and grammar skills.

Conclusions: The MNREAD test is reliable and valid for use in children with vision impairment.

Translational Relevance: The MNREAD test can be utilized by clinicians as it is a quick, easy to administer method to evaluate reading vision in children with VI.

Introduction

Much of what we know about the visual requirements for reading with normal or impaired vision comes from the work of Legge and colleagues.[1] In adults, we know that the integrity of the central visual field accounts for the largest portion of the variance in reading speed.[2] However, most of the adults with vision impairment in those studies learned to read before they developed vision impairment. The majority of children with vision impairment have enough sight to read visually and do not learn to read Braille.[3, 4] After an extensive literature search, the fastest mean maximum oral reading rate found in a study of children with vision impairment was 147 ± 61 words per minute (wpm).[5] The reading rate in that study increased by 9.9 wpm per year of age, in contrast to normative data from Carver[6] where the reading rate of children with normal vision increased by 14 wpm per year of age. There are several additional studies supporting the finding of decreased reading rates among children with vision impairment.[7-11] Because reading rates will vary depending on many factors (age and grade of child, text size, difficulty, length, mode of presentation, type of reading: oral versus silent, skimming versus reading each sentence for comprehension), there is no gold standard "normal" reading rate for children or adults. Studies using a normally sighted control group provide the best comparisons, as the testing situations are the same.

The MNREAD acuity charts are commercially available reading speed and acuity tests that are increasingly being used to measure outcomes after medical treatment for eye disease such as diabetic retinopathy,[12] retinal vein occlusion,[13] macular hole or pucker[14] or to evaluate medical devices such as multi-focal intraocular lens implants.[15] The MNREAD has also been used to determine effects of vision

rehabilitation in adults.[16, 17] Despite its benefits, the use of the MNREAD in children has been limited[11, 18, 19] and the repeatability and validity of the English Version has yet to be studied in children with low vision. The MNREAD Acuity Charts use sentences of 10 standard word length (60 characters) to determine reading speed across print sizes that decrease logarithmically from ranging from 8M (11.6 mm x-height) to 0.13M (0.19 mm x-height). This corresponds to a range from 20/6 (-0.5 logMAR) to 20/400 (1.3 logMAR) when tested at 40 centimeters. Testing with the MNREAD Acuity Charts yeilds 3 reading performance measures: maximum oral reading rate, reading acuity (smallest print size read) and critical print size (smallest print size read at the maximum reading rate). More recently, a reading accessibility index has been developed to provide a single measure that reflects an individual's ability to access print.[20] The purpose of our study was to investigate the test-re-test reliability as well as the validity of the MNREAD acuity charts in children with and without vision impairment.

Methods

This study was approved by the University of Alabama at Birmingham Institutional Review Board for Human Use and adhered to the tenets of the Declaration of Helsinki. A parent or guardian provided written informed consent. Children aged 14 and older also provided written informed consent, whereas younger children provided written assent.

Participants

Children with VI not correctable with glasses or contact lenses were recruited for participation from the UAB Center for Low Vision Rehabilitation. Children with normal vision were recruited through flyers placed in the Center's waiting room. Children in 1rst through 12th grade were invited to participate. Inclusion criteria for children with VI were bilateral VI of organic etiology and best-corrected visual acuity in the better eye between 0.3 and 1.6 logMAR (20/40 to 20/800). Inclusion criteria for children with normal sight were best-corrected visual acuity in each eye of at least 0.1 logMAR (20/25 or better), and refractive error between +4D and -4D with no more than 1.5D astigmatism or 0.75D anisometropia. Exclusion criteria for both groups included diagnosis of a reading disability, total standard score on the Slosson Intelligence test of less than or equal to 85 or the inability to read at a third grade independent level on the Word Reading test of the Jerry John's Basic Reading Inventory.[21] This reading level was chosen, as the MNREAD sentences are comprised of words from the 1000 most common words found in 3rd grade schoolbooks.[22]

Procedures

Parents provided information about birth history, ocular diagnosis, medical conditions, medications and school (grade, accommodations and services). Visual acuity was measured using the EVA electronic visual acuity tester (Jaeb Center for Health Research, Tampa, FL) at a 3 meter test distance using the standard protocol[23] after best-correction. Acuity was measured OD, OS and OU. EVA scores were converted to logMAR with the following formula: 1.7 – (0.02)(letter score).

MNREAD testing was conducted binocularly using the patient's habitual correction for reading and the MNREAD Acuity Charts 1 and 2 (Precision Vision Inc, LaSalle, IL). Two reading conditions were used for participants with VI: fixed 20 cm distance or preferred distance. For preferred distance testing, participants with VI were permitted to get closer to the card as needed in order to read the print. Participants with VI were randomized to use either chart 1 or chart 2 at a fixed 20cm distance; the remaining card was tested at their preferred distances. Only data for the 20cm fixed test distance is presented here. The order of testing was also randomized. Participants with normal vision read both charts 1 and 2 at the fixed 20cm distance, but the order of presentation was randomized. The card was placed on a reading stand and the 20cm testing distance was maintained through the use of strings attached to the card. Sentences were covered and revealed one at a time during testing. Participants were instructed to read each sentence as quickly as possible without making mistakes, but if they did make a mistake not to fix it but rather to finish reading. A second examiner timed the passage reading and recorded results to the nearest 0.1 second as well as errors.

The following parameters were determined for the MNREAD: maximum oral reading rate (MRR), critical print size (CPS) and reading acuity (RA) as recommended in the test instructions, accounting for errors. Maximum oral reading rate was determined as the mean of the 3 fastest reading speeds. The smallest print size that could be read at 90% of the maximum reading rate was designated the CPS. RA was the smallest print read adjusted for errors. The MNREAD cards are labeled for a 40cm reading distance, and were adjusted by 0.3 logMAR since the test was done at 20cm.

The Basic Reading Inventory (BRI) is a test used in the educational setting and was chosen to assess the validity of the MNREAD because it is straightforward to administer and is not used in the school districts where we recruited participants. The test offers both word reading lists to determine reading level (through 12th grade) and graded word passages (through 8th grade). In this test, students were asked to choose between a regular print version (ranges from an x-height of 2.25 mm for 3rd grade lists/passages to 1.75 mm for 8th grade passages) and a large print version (6-7mm x-height for all passages). Participants were permitted to hold the print at their desired working distance, as would be done in the school setting. Words read per minute were calculated using standard length words (a standard length word is 6 characters long) as recommended by Legge[1] rather than the actual word count. The independent reading level was determined for word reading lists as well as graded passages per the instructor manual. The highest passage reading level in the BRI is 8th grade.

MNREAD and BRI testing was repeated one to three weeks later, according to the same randomization scheme, administration and scoring protocols as were used at the initial visit.

Data Analysis

Data was analyzed using SAS (version 9.4 SAS, Cary, NC). Figures were created with Prism 8 form Mac (GraphPad Software, San Diego, CA). T-tests and Chi-square tests were used to detect differences between children with and without vision impairment for continuous and categorical data, respectively. Test-retest repeatability was measured using intra-class correlations. Bland – Altman plots were used to graphically evaluate differences between test and retest values. Linear Regression was

used to determine the relationship between grade and reading speed. Significance was set at $p < 0.05$, 2-tailed.

Results

Letters were sent to 99 parents of children with VI in grades 1 through 12 who were patients of the first author and who did not have a history of developmental delay or cognitive impairment. Of those, 78 agreed to participate. Forty-four children with normal vision were enrolled, one was screened out due to diagnosis of dyslexia. Sixteen children with VI (8 of whom were in 1rst or 2nd grade) and 4 children with normal vision were excluded from analysis due to inability to read 3rd grade word lists on the BRI at an independent level and/or total standard score on the Slosson Intelligence test of 85 or less. No children in 1rst grade were included in the analysis, however 3 of 6 second graders with VI met inclusion criteria. There were 62 children with vision impairment and 40 children with normal vision who met entry criteria and were included in these analyses. The children with VI were similar to children with normal vision with respect to age, gender, race, intelligence and number of adults in the household (Table 1). However, children with VI were more likely to live in a household with income of less than $30,000 per year.

Table 1: Demographic characteristics of study population

	Participants with Vision Impairment (N=62)	Participants with Normal Vision (N=40)	p-value
Age (mean, (SD))	13.3 (3.0)	13.3 (2.6)	0.99
Gender (n, % male)	40 (64.5)	20 (50.0)	0.15
Race (n, %)			
White	42 (67.7)	30 (75)	0.7
Black	15 (24.2)	8 (20.0)	
Other	5 (8.1)	2 (5.0)	
Premature Birth (n, %)	7 (11.3)	5 (12.5)	0.9
Screening Intelligence Total Standard Score (mean, (SD))	107.9(14.5)	106.3 (12.4)	0.6
School Setting (n, %)			
Public	38 (61.3)	30 (75.0)	0.01*
Private	10 (16.1)	2 (5.0)	
Homeschool	5 (8.1)	8 (20.0)	
School for the Blind	9 (14.5)	0 (0.0)	
Receives special services at school			
No service or accommodations	3 (4.8)	40 (100.0)	<0.01*
Accommodations but no direct services	30 (48.4)	0 (0.0)	
Direct services of non-vision specialist	3 (4.8)	0 (0.0)	
Direct services of TVI	8 (12.9)	0 (0.0)	
Direct services of TVI & mobility specialist	7 (11.3)	0 (0.0)	
Extensive services at school for the blind	9 (14.5)	0 (0.0)	
Orientation and mobility services only	2 (3.2)	0 (0.0)	
Uses an electronic video magnifier at home (n, %)	24 (38.7)	0 (0.00)	<0.01*
Family income			
Less than$29,999	14 (22.6)	3 (7.5)	0.01*
$30,000 or more	46 (74.2)	29 (72.5)	
Decline to answer	2 (3.2)	8 (20.0)	
Number of adults in household			
1 (n, %)	10 (16.1)	4 (10.0)	0.4
2 or more (n, %)	52 (83.9)	36 (90.0)	
Number of children in household (mean, SD)	2.1 (0.9)	2.7 (1.3)	0.004*

TVI = teacher of the visually impaired

Table 2 details the visual characteristics of the participants. Albinism was the most frequent cause of VI, followed by retinal dystrophies or degenerations and optic atrophy.

Table 2: Visual Characteristics of study population

	Participants with Vision Impairment (N=62)	Participants with Normal Vision (N=40)	p-value
Ocular Diagnosis			
Achromatopsia, cone dystrophy	7 (11.3)	0 (0.0)	< 0.001*
Albinism, congenital nystagmus	27 (43.6)	0 (0.0)	
Optic atrophy	8 (12.9)	0 (0.0)	
Optic nerve hypoplasia	4 (6.5)	0 (0.0)	
Other	6 (9.6)	0 (0.0)	
Retinal degeneration/dystrophy	8 (12.9)	0 (0.0)	
Retinopathy of prematurity	2 (3.2)	0 (0.0)	
None (control)	0 (0.0)	40 (100.0)	
Best-corrected distance visual acuity (logMAR)	0.7 (0.2)	-0.08 (0.05)	<0.001*
OD (mean (SD))	0.7 (0.3)	-0.09 (0.05)	<0.001*
OS (mean (SD))	0.6 (0.2)	-0.12 (0.04)	<0.001*
OU (mean (SD))			
Reading acuity OU (logMAR)	0.57 (0.23)	-0.15 (0.10)	<0.001*
Nystagmus (n, %)	41 (67.2)	0 (0.00)	<0.001*
Mars Contrast Sensitivity (mean (SD))	1.6 (0.2)	1.8 (0.05)	<0.001*

Two-thirds of the VI group had nystagmus. The mean best-corrected binocular visual visual acuity was 0.6 ± 0.2 logMAR (20/80) for children with VI and -0.13 ± 0.04 (20/15) for children with normal sight. Children with normal sight also performed better on contrast sensitivity testing.

Difference versus mean plots (Bland and Altmann) are presented for RA, CPS, MRR and Basic Reading Inventory Reading Rate for the entire sample in order to illustrate test-retest relationships (Figure 1). None of the slopes were significantly different than zero, suggesting no systematic bias between the measurements. There is very strong agreement overall between test and retest values for RA, CPS, MNREADMRR and Basic Reading Inventory grade level and MRR (Table 3).

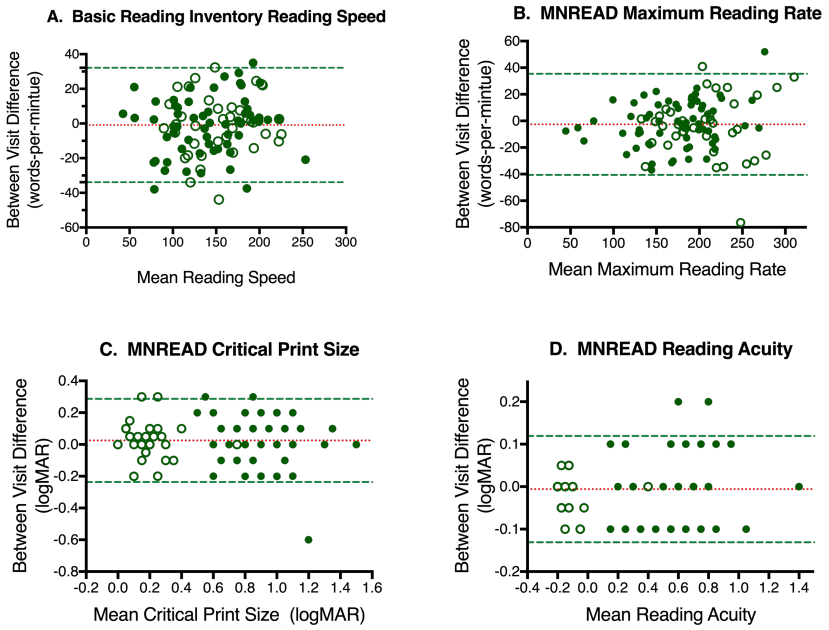

Figure 1: Difference versus means plots (Bland-Altmann) comparing results from visit 1 and 2. Open circles denote participants with normal vision and closed circles denote participants with VI. Red dotted lines indicate the mean difference between the two measures. The green dashed lines indicate +/- 1.96 SD

Table 3: Intraclass correlations for test –retest.

	MNREAD Reading Acuity	MNREAD Critical Print Size	MNREAD Maximum Reading Rate	Basic Reading Inventory Reading Rate
Overall	0.99	0.95	0.94	0.93
VI	0.95	0.77	0.94	0.93
Control	0.93	0.68	0.93	0.91

Comparing children with VI to those without VI, there are significant between groups differences in RA and CPS as the groups were designed to differ in visual ability (Table 4). Although children with VI on average read slower on both the MNREAD and the BRI, the difference was only statistically significant for those in grades 9-12. As expected, both RA and CPS were significantly different ($p<0.001$) between participants with and without VI across all age groups.

Table 4: Comparison of MNREAD values and Basic Reading Inventory (BRI) maximum reading rates between children with and without vision impairment by grade levels. Average values for each participant over the 2 visits were used for comparisons

Grade	Reading Acuity [mean, (SD)]		Critical Print Size [mean (SD)]		MNREAD Maximum Reading Rate [mean (SD)]			BRI Maximum Reading Rate [mean (SD)]		
	VI	Control	VI	Control	VI	Control	p-value	VI	Control	p-value
2-5	0.59 (0.17)	-0.16 (0.05)	0.95 (0.19)	0.23 (0.07)	146.5 (44.1)	180.6 (34.1)	0.06	111.1 (26.0)	124.9 (24.0)	0.2
6-8	0.58 (0.23)	-0.12 (0.15)	0.89 (0.24)	0.23 (0.16)	183.6 (54.8)	191.2 (39.5)	0.66	147.4 (57.9)	143.3 (38.6)	0.82
9-12	0.58 (0.26)	-0.18 (0.04)	0.89 (0.22)	0.13 (0.07)	183.0 (45.9)	236.8 (34.3)	<0.01*	157.1 (40.2)	181.8 (29.0)	0.04*
All grades	0.57 (0.23)	-0.15 (0.10)	0.90 (0.21)	0.19 (0.12)	171.7 (48.9)	205.9 (43.2)	<0.01*	140.3 (45.4)	153.6 (39.1)	0.13

To assess the validity of the MNREAD test, we compared the reading rates from the MNREAD and the BRI. While the values are strongly correlated (Pearson r = 0.88), they are still significantly different both overall and when grouped by vision status. The MNREAD tests yields faster reading speeds than the BRI. Reading speeds on the MNREAD were 31.4 ± 21.5 wpm faster for children with VI and 52.3 ±19.5 wpm faster for children with normal vision than reading speeds on the BRI.

When looking at reading speed by grade level, among children with vision impairment, on average reading speed increased 4.4 wpm (95% CI 0.3 to 8.4) on the MNREAD test and 5.9 wpm (95% CI 2.4 to 9.5) on the Basic Reading Inventory each year. Children without vision impairment increased 10.6 wpm (95% CI 6.2 to 15.0) on the MNREAD test and 9.7 wpm (95% CI 5.8 to 13.7) on the Basic Reading Inventory each year. (Figure 2)

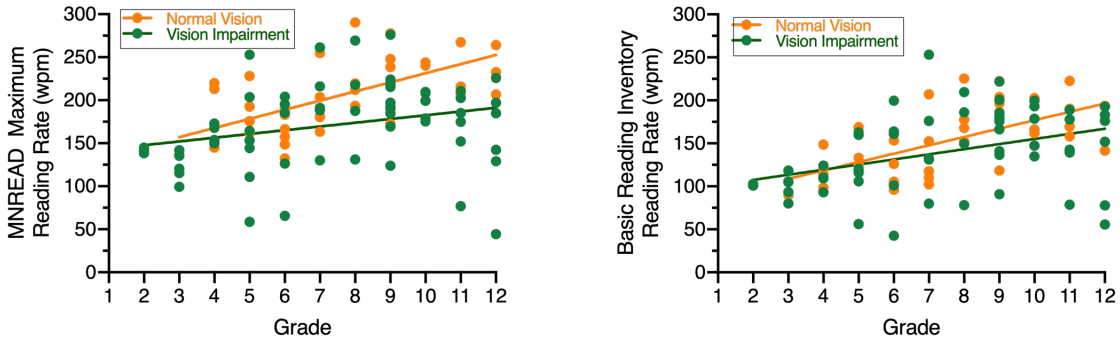

Figure 2: Reading speed in words per minute (wpm) by grade for the MNREAD test (left) and Basic Reading Inventory (BRI – right).

The association between best-corrected visual acuity and reading speed for both the MNREAD test and the Basic Reading Inventory (reading speed for each test averaged over the 2 visits) was investigated using univariate regression (Figure 3). There was a significant association between poorer visual acuity and lower reading speeds on the MNREAD test (Pearson r= -0.26, p= 0.04) but not on the Basic Reading Inventory (Pearson r= -0.13, p=0.3).

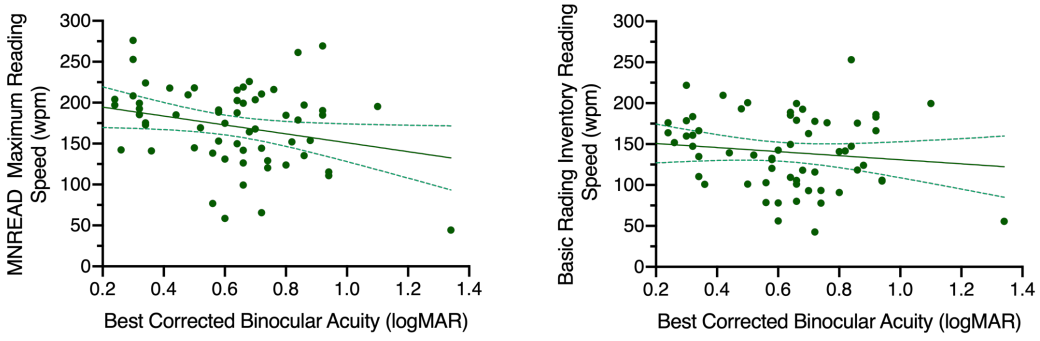

Figure 3: Relationship of reading speed for the MNREAD test (left) and Basic Reading Inventory (right) to visual acuity for participants with vision impairment. (WPM = words per minute). Dotted lines indicate 95% confidence interval.

Discussion

The MNREAD test shows good test-retest reliability for children with VI and with normal vision. CPS varied the most from visit 1 to visit 2, with the majority of results within 0.2 logMAR (2 lines of print size). Reading speed is highly variable from person to person, however the ICC was excellent for both reading tests. These results are similar to those of Virgili et al[18] who examined the use of the MNREAD test in Italian children with normal vision and Subramanian and Pardhan[24] who examined it in adults with low vision.

The MNREAD reading speeds in our study were similar to those of Calabrese et al[25] who found that at age 8 children read on average 137 wpm and increased by 8.13 wpm/year until they were age 16 when their reading speeds plateaued around 202 wpm. The children without VI in this study exceeded the reading speeds in her cohort and increased their reading speeds by more words per year. However, although younger children read similarly to their normally sighted peers, the older children with VI did not reach 202 wpm. This is not surprising as reading speeds in our VI group increased annually by half of that of Calabrese's cohort. These students with VI did not reach a plateau in reading speed, unlike those of Corn et al[9] who found that reading speeds plateaued under 100 wpm after 6th grade among readers with VI.

The MNREAD maximum reading speed, is an average of the 3 fastest reading speeds on the test and is much faster than the reading speeds on the BRI. The BRI is a paragraph reading test, and as such the reading rates would not be expected to be identical between the 2 tests. However, the strong correlation between the 2 tests supports the validity of the MNREAD test. It is well known that the type of reading being done

impacts reading speed. Several possibilities exist as to the reason why reading speeds are greater on the MNREAD test. First, the MNREAD is short enough that the reader does not need to take a breath during reading of the sentence and they are instructed to read as quickly and accurately as possible.. Second, readers may become fatigued over the course of reading the paragraph. Adult readers with glaucoma have been shown to read more slowly on longer passages.[26] Third, the reader may be slower as they try to comprehend the paragraph (although no instructions regarding comprehension were given and no comprehension questions were asked). Fourth, the passages being read on the BRI were at the child's independent reading level up to the 8th grade level which is the maximum for the test, so the complexity of the passage may have been greater.

Two-thirds of the participants with VI in this study had nystagmus and one might attribute slower reading speeds among the VI group to nystagmus. However it has been shown that people with nystagmus are reading during non-foveating periods.[27] This was further supported by Dysli and Abegg[28] who found that although latency to initiating reading of an 8-letter word was longer, first fixation duration was shorter and the number of fixations were greater among participants with nystagmus. Text reading speeds were the same as healthy controls. Wang and Dell'Osso[29] described the concept of children with nystagmus being "slow to see". They found that the oculomotor system utilizes foveating and braking saccades to adapt to the underlying nystagmus and that the foveation periods following foveating saccades facilitate how well the person sees. They propose that these periods have a negative effect on how quickly they see making target acquisition time an additional factor in visual function.

The concept of being "slow to see" could explain why there are greater percent differences in reading speed between readers with VI and normal sight on the MNREAD test versus the BRI. Although in general, the VI readers do read faster on the MNREAD than the BRI, they may be "slow to see" and therefore take longer on a shorter passage than their normally sighted counterparts who are able to begin as soon as the sentence is revealed. These shorter sentences likely reflect differences in their ability to percieve the stimulus, whereas the longer passages would be more dependent on other skills such as grammar and linguistics.[28, 29] Despite the differences between children with and without VI, reading speeds in this group of children with VI are faster than those reported in the literature.

A strength of this study is that the participants were screened to be sure that they were not cognitively impaired and that they were able to read at an independent reading level of at least grade 3. Some causes of pediatric low vision such as septo-optic dysplasia[30] or retinopathy of prematurity[31] are associated with other disabilities, and having vision impairment does not protect a child with low vision from having a reading disability. By restricting enrollment to those without cognitive or reading deficits we are able to measure reading speed without those potential confounders. Additionally, 62 children with VI is a large sample size given the prevalence of pediatric VI in the US population.

Conclusion

The MNREAD test shows good test-retest reliability and criterion validity. It is useful in the evaluation of reading in children with VI, but should be interpreted with caution as it may over-estimate reading ability for longer passages. As the critical print

size is the most variable parameter across visits, it may be necessary to determine the CPS on more than one occasion before using this information to recommend print sizes for educational purposes.

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CHAPTER 6: DISCUSSION

The importance of studying children with vision impairment cannot be over-estimated. When VI begins in childhood, it has a lifelong impact. It is clear that we do not have an evidence base upon which to guide clinical practice for the rehabilitation and education of children with VI. This work provides a basis for 3 possible outcome measures for use in intervention trials in this population. It also provides insight into problems encountered by children with VI.

The children who participated in these studies had a variety of causes for VI, primarily of a congenital and/or hereditary nature. These conditions are representative of those found in various surveys of causes of VI among children in schools for the blind or other studies specifically studying childhood VI. Because the incidence of permanent, uncorrectable VI in children is so rare, population-based epidemiological studies such as the MEPEDS [142] or BPEDS [11] do not give us guidance as to the actual distribution of causes. Our studies purposefully excluded children with multiple disabilities as the goal was to ascertain the impact of VI, and including children with conditions such as cerebral vision impairment or VI with concomitant cerebral palsy would add confounders that would likely affect study outcomes. Therefore, we included children whose only disability was VI.

Quality of Life

Quality of life is impacted by vision impairment, primarily in the psychosocial domain. This was evidenced by both our previous work using focus groups[35] and the work described here using the Peds QL™ 4.0. QoL scores were 8 to 20 points higher for children with normal vision than children with VI across all domains except physical functioning and by both parent and child report. In general, children rated their QoL higher than parents. Additionally, the impact of VI on QoL is related to visual acuity. In future intervention studies, the Peds QL™ 4.0 would be an appropriate instrument to use as a patient reported outcome measure (PROM) as we have shown it to have excellent internal consistency reliability and to be able to discriminate between groups of children with and without VI. While it may be intuitive that VI would impact QoL, it is important to identify an instrument that can reliably do so in children as the patient's perspective has become increasingly important in clinical vision research [143]. Although PROMs are often used as secondary outcome measures, in some low vision rehabilitation trials they are used as the primary outcome measure [144, 145]. PROMs are of paramount importance in any intervention trial. Having an appropriate measure to obtain the patient and their parent's perspective is important since if we only find improvement in clinical values, without subjective improvement for the person, the intervention may not be the most appropriate. Conversely, if two interventions are found equally efficacious in this population, a PROM may help to determine which is more appropriate.

Accommodation

Young children whose distance refractive error is corrected must accommodate to see clearly at near. It is well known that slight under-accommodation to near targets is normal. However, the children with VI in this study tended to under-focus near targets both by a clinical test of accommodative accuracy (Nott dynamic retinoscopy) and a gold standard autorefraction (open field autorefraction with the Grand Seiko WAM 500) by on average approximately twice on average that of the normally sighted control group. The test-retest reliability was greater for the WAM 5500 than for the Nott retinoscopy, supporting its use in research on near focusing in children with VI. However, the trends with Nott retinoscopy were the same and this research supports its use as a clinical test in children with VI as most clinicians do not have access to an open field autorefractor. Although some may argue that since there is increased blur tolerance among children with low vision an increased lag of accommodation would be expected and not harmful. While this is true for lower lags, some participants appeared to accommodate very little if at all. This means that for at least some children with vision impairment poor accommodation likely does affect their near task performance, especially reading. Since poor accommodative ability is remediable with plus lenses at near, it is important to be able to discern which children need them.

Reading

The goal of this paper was to validate the use of the MNREAD in children with VI. That goal was achieved with strong intraclass correlations for test-retest values for reading acuity, critical print size and maximum reading rate as well as strong correlations

with an educationally based test, the Jerry Johns Basic Reading Inventory. The data collected for this aim also afforded an opportunity to look further into reading across grades for children with VI. Unlike Corn et al's study[106], we did not find a plateau in reading ability although the slope of change for children with VI was less than that of the children with normal vision (4.4 versus 10.6 wpm/year). Since the disparity was less for the Jerry Johns Basic Reading Inventory (5.9 vs 9.7 wpm/year), this study also confirms in children that the MNREAD is a measure of their ability to see the stimulus whereas the longer passage is also affected by other factors such as linguistics. The MNREAD which contains 10-word sentences is a useful instrument for studies of reading in children with VI, however researchers interested in more than the purely psychophysical aspects of reading should also consider using a longer consider using a task that includes longer reading passages. Children with VI, like their normally sighted peers have a wide range of reading abilities. Given the low incidence of pediatric VI in the population, many studies do not screen out children with lower intellectual ability. By limiting eligibility to children with screening IQ $\geq$ 85, our sample included only those without intellectual disability, similar to that of the control children. The fastest reading speed of all participants on the Jerry Johns Basic Reading Inventory was achieved by a child with VI. So, VI in and of itself does not rule out normal or even very fast reading speeds. This means that we need to further investigate WHY some children with VI read much more slowly than their normally sighted peers while others become excellent readers.

Limitations

These studies have two main limitations. First, all participants were from a single clinic in Birmingham, Alabama and may not be representative of children with VI in other parts of the country or world. Second, although the sample size was large compared to other studies on children with VI, the sample size was not large enough to do stratified analysis based on eye condition or visual acuity.

Summary

Each experiment in this dissertation was designed to contribute to answering the clinical dilemma of how to best prescribe adaptive equipment for children with VI. Some clinicians believe that for the most part children with VI do not need adaptive equipment as they simply hold things closer to achieve relative distance magnification. The rationale is that the image of an object that is moved 2 times closer will subtend an angle on the retina that is twice as large as when it was at the original location; four times as close then the image is four times as large, and so on. By increasing the retinal image size through relative distance magnification, there is theoretically no need for other forms of magnification. However, the studies presented in this dissertation have shown that simply allowing children with VI to hold things closer in order to see them may work for some, but is likely not ideal for others. The QoL of children with VI is affected especially with regards to psychosocial aspects. Their primary means of coping with their impairment therefore is not adequate as they still related difficulties in many areas including keeping up in school or doing things their friends could do. We also know that using relative distance magnification is going to be most effective if the child has the

accommodative accuracy to keep the image clear at the closer distance, but many children with VI do not have that ability. Lastly, we know that some readers with VI are quite fast while others are slow. We have not yet discovered the reason why some read more slowly but our results suggest that the vergence system may play a role. We have shown that reading speed is not mediated by visual acuity alone. Clinicians can use this information to encourage educators to seek other causes of reading difficulty such as a reading disability.

When determining the best rehabilitation plan for a child with VI, all of the above must be considered. A child already struggling with social and emotional issues related to their VI may be less likely to accept a rehabilitation strategy that will make them look even more different than their peers. For example, in some schools, children with VI use a video magnifier (also known as a CCTV) that the child must push on a cart from class to class. Many reject this device simply because they feel it garners unwanted attention from other children and emphasizes the difference between them and their peers. A child who has a large lag of accommodation may benefit from reading glasses, or if they are already wearing glasses, from a bifocal correction. The MNREAD determines a child's critical print size (the smallest size print that facilitates reading rates near their maximum reading speed) so that clinicians can recommend appropriate enlarged print sizes or to help determine the amount of magnification needed to provide optimal access to print. Measuring quality of life, accommodation and reading are important foundations for developing a rehabilitation plan for children with VI.

Future Direction

The three studies that comprise this dissertation are all related not just because they were done with children who have impaired vision, but also because the results of one may impact or be impacted by the other. For example, the ability to read is associated with educational success. Lack of success can affect QoL. Poor near focusing may impact the ability to read. Planned future work includes evaluating other factors that may influence reading in children with VI.

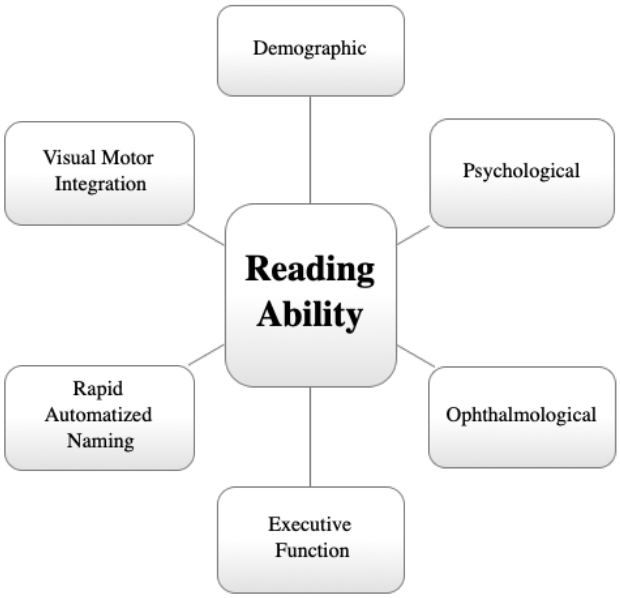

Figure 4: Proposed areas of study affecting reading ability

Clinical trials involving interventions with adaptive equipment such as optical or video magnifier should include measures of the impact on QOL as well as reading ability. The more we know about how children with VI function, the better we can design and test interventions. To achieve optimal sample sizes, it is likely that these studies will need to be multi-center.

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APPENDIX

INSTITUTIONAL REVIEW BOARD APPROVAL LETTER

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM
Office of the Institutional Review Board for Human Use

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Birmingham, AL 35294-0104
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APPROVAL LETTER

TO: DeCarlo, Dawn Kissner

FROM: University of Alabama at Birmingham Institutional Review Board
Federalwide Assurance # FWA00005960
IORG Registration # IRB00000196 (IRB 01)
IORG Registration # IRB00000726 (IRB 02)

DATE: 05-Dec-2019

RE: IRB-130204001
Accomodation and Reading (Reading and Pediatric Vision Impairment)

The IRB reviewed and approved the Continuing Review submitted on 03-Dec-2019 for the above referenced project. The review was conducted in accordance with UAB's Assurance of Compliance approved by the Department of Health and Human Services.

Type of Review:	Expedited
Expedited Categories:	4, 7
Determination:	Approved
Approval Date:	05-Dec-2019
Approval Period:	One Year
Expiration Date:	04-Dec-2020

The following populations are approved for inclusion in this project:

- Children

The following apply to this project related to informed consent and/or assent:

- Waiver (Partial) of HIPAA

Documents Included in Review:

- IPR.track.191203
- response.191203
- ipr.clean.191203