Development of Form Visual Acuity in Infants Measured by Schematic Faces

by

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AUTHOR'S DECLARATION

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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Abstract

Purpose

The purpose of this thesis was 1) to develop a test of visual acuity (VA) to measure recognition (form) acuity at a younger age than is currently clinically possible (3 years). Currently, it is only possible to measure resolution (grating) VA in this age group. 2) To validate infant's recognition VA tests against gold standard ETDRS VA in adults. 3) To test the feasibility of using infant's recognition VA tests to measure VA in infants 16 - 42 months of age in terms of the testability and ability to measure VA.

Methods

Preliminary study 1 – Development of Face targets: Adults participated and visual acuity for various versions of face targets were tested under blur in comparison to ETDRS or Tumbling E optotypes. The face targets were successively modified in six trials until the optimal agreement with ETDRS and Snellen Tumbling Es was obtained.

Preliminary study 2 (Infants aged 3-15 months): In experiment 1, suprathreshold pairs of targets consisting of happy faces vs scrambled faces or happy faces vs dotted-target were presented either on preferential looking cards or on a computer screen with a non-contact gaze tracker. Percent accurate fixation towards the face compared to the non-face was observed by

a naïve observer. In a second phase, habituation for the non-face stimuli were used in which the non-face target was presented twice before each face/non-face pair.

Validation study (adults): A series of acuity cards with logarithmic progression in spacing and size (1.3 to -0.1 logMAR) designed for a 60 cm test distance was created. The Face Cards had a smiley face and a dotted target as optotypes. Patti Pics Cards used the house and the circle. Recognition VA was measured with Face Cards, Patti Pics Cards, and near ETDRS chart monocularly, in a counter-balanced order under 3 conditions of optical blur; +4.00D, +2.50D and no blur.

Feasibility study (infants aged 16-42 months): Testability and form VA threshold were measured in infants on 2 visits using the Face Cards and Patti Pics Cards in a counter-balanced order. After initial training to point at the target stimulus (face or house), testability was measured using 30M target size with 3/4 correct responses as the criterion to be considered testable. If the infant was testable, two alternative forced choice VA measurement followed using a two down one up staircase procedure. For reference, testability for matching with the Patti Pics and VA with the Cardiff cards were measured.

Results

Preliminary study 1 – Development of Face targets: The modified border simple face was chosen as most suitable in terms of its apparent appeal as a face and similar results to ETDRS and tumbling Es.

Preliminary study 2: Infants aged 3-15 months Eight infants took part in Phase 1 (median age 10.5 months, range 8.5 – 14 months). The percentage of correct looks with the eye tracker was not significantly different from 50% with either the cards or the eye tracker. Eleven infants participated in Phase 2 (median age 11.5 months, range 3.5 – 15 months). Percent correct looks was not significantly better with habituation.

Validation study (adults): Twenty-two participants took part in this experiment, age range was 22 - 35 years, median age was 27 years. Repeated measure ANOVA showed a significant effect of VA method for all levels of blur ($p<0.05$). Post-hoc analysis showed that Patti Pics Cards gave significantly better VA than ETDRS and compared to Face Cards, but there was no significant difference between Face Cards and ETDRS. The same pattern of differences was found for all levels of blur.

Feasibility study: (infants aged 16-42 months): Seventeen infants took part in this study, median age was 27 months. Testability of Face Cards was 70.5%, while the testability of the Patti Pics Cards and matching Patti Pics were both 64.7%. All participants aged ≥26 months could perform all three tests, including a VA result. Among infants in whom a measure of VA was obtained, a significant difference was found between Face Cards and Cardiff Cards (mean difference 0.35 logMAR, $p=0.0007$) and between Patti Pics Cards and Cardiff Cards (0.2 logMAR, $p=0.049$), while no significant difference was found between Face Cards and Patti Pics Cards (0.15 logMAR, $p=0.15$). Correlation between age and VA was; Face Cards $r = 0.76$ ($p = 0.006$), Patti Pics Cards $r = 0.8$ ($p = 0.003$), Cardiff Cards $r = 0.72$ ($p = 0.001$).

Conclusion

The preference for faces, even with habituation, was not sufficiently strong in babies aged 3 – 15 months to use for recognition visual acuity measurement. A pointing paradigm appears to have potential for children between 26 months and 3 years with either Face/non-face targets or Patti Pics symbols. However, in adults, Face Cards give VA more similar to ETDRS acuity than Patti Pics Cards and may provide a valuable alternative method for measuring recognition VA in young children. Recognition acuity increased with age over the infant range at a faster rate than resolution acuity.

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Dedication

To my parents,

Amal and Hamad Alkanhal

Without whom none of my success would be possible

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Chapter 1- Introduction and Literature Review

1.1 Visual Acuity

Visual acuity (VA) is a measure of the visual system's ability to resolve detail. It is the most commonly used tool to assess visual function. It is usually measured under high illumination and high contrast conditions. It is a measure of the minimum angle of resolution (MAR) in minutes of arc for which the person can perform the task. Thus, it is a measure of the resolution of the eye and visual system.

1.1.1 Importance of measuring visual acuity in infants

Visual acuity is often considered one of the most important measures of visual function. It is used to detect and monitor diseases and injuries affecting the eye and the visual system. In infants, accurate measurement of visual function is essential since no symptoms can be obtained. Common conditions affecting an infant's visual acuity include; high refractive error that affects 4 – 14% of children[1] and amblyopia with a prevalence of 1.8%.[2] Amblyopia can be caused by untreated refractive error or strabismus but also any untreated ocular condition that obstructs visual input to the brain can cause amblyopia in children. Amblyopia is easily detected when VA is assessed and monitored regularly. Prevention of amblyopia is usually possible when the causative condition is treated early. Once established, treatment is possible in many cases, although amblyopia may not be completely eliminated and treatment becomes more difficult with increasing age.

1.1.2 Types of visual acuity tests

There are four different tasks that are used to measure four different types or aspects of visual acuity.[3] First, detection acuity: this measures the ability to detect the presence of a stimulus. One way of measuring this type is presenting beads in decreasing sizes to the patient until they can no longer detect their presence. The threshold from this measurement can be as small as 0.5 seconds of arc.[4] Second, resolution acuity: this measures the ability to resolve two different stimuli i.e. to determine that there are two stimuli and not one, e.g. a black and white grating. It is measured clinically using black and white stripes decreasing in width until the patient can no longer resolve them, and the stimulus appears as a homogenous grey area. Clinically, this task is usually done in preferential looking format (PL)[5,6] and used for patients who are too young to perform a recognition acuity task (described below). Resolution acuity typically is recorded in cycles per degree (cpd) (30 cpd has a 1 minute of arc gap between the bars and is therefore this gap is equivalent to that of a 6/6 letter). A typical adult resolution VA is 40 cpd.[7] Third, recognition acuity: the ability to identify optotypes (letters, numbers, or symbols) of decreasing size. The optotypes can be presented one at a time, or in a full chart which introduces the crowding phenomenon. Crowding is defined as the impact of surrounding contours on the ability to recognize an optotype.[8] Typically, adults can correctly identify optotypes of 0.8 minutes of arc detail size at 6 meters (20ft), which is approximately -0.1 logMAR.[7] Crowding makes the task more difficult i.e. reduces visual acuity. Recognition acuity can be recorded in many ways, most commonly with the Snellen fraction (see 1.1.3.1). Lastly, hyperacuity: this is the measurement of the minimum difference in position between two stimuli that the visual system can detect or discriminate e.g. vernier acuity and stereo acuity. The visual system can discriminate differences in position as small as 3 seconds of arc.[9] These different tasks result in different measures of acuity, are not always highly correlated and are affected by visual anomalies and diseases to different extents.

1.1.3 Testing visual acuity in adults

1.1.3.1 Snellen chart

Recognition visual acuity tests were first designed by H Snellen.[10] He used full contrast Roman letters decreasing in size using angular sizes to calibrate the chart. The detail of the letter (or the stroke width of the letter) is 1/5 of the whole letter size. The patient's task is to read the letters as they get smaller until he/she can no longer correctly identify the letters. Snellen introduced the "Snellen fraction" that describes the optotype angular size, to be used in recording the smallest optotype that the patient can see. The fraction is written as follows: the distance at which the test was performed divided by the distance at which the whole optotype subtends 5 minutes of arc i.e. the distance at which the detail subtends 1 minute of arc. Consequently, a whole letter on the 6/6 line subtends 5 minutes of arc. The disadvantage of the original Snellen chart is the different number of letters on each line and asymmetrical spacing between lines and letters, which makes the task vary in difficulty among the lines. With respect to the total size of the letters, smaller lines were packed more closely than the bigger ones, which increases the task's difficulty as the letters get smaller. This is because there is more crowding when the letters are closer with respect to their size.

1.1.3.2 Bailey-Lovie and Early treatment diabetic retinopathy study (ETDRS) charts

These charts were designed so that the letters follow a logarithmic scale in 0.1 log steps per line and have 5 letters in each line. The spaces between letters and the spaces between lines are proportional to the size of the optotypes, meaning that there is also a logarithmic scale in spacing resulting in equal legibility among all lines and optotypes. This approach was first proposed by Green.[11] The Bailey-Lovie chart[12] has 10 different letters of equal legibility (British Standard letters: D, E, F, N, H, P, R, U, V, Z). The ETDRS chart was developed by Ferris et al.,[13] and the letters in this chart are limited to the 10 Sloan letters (C, D, H, K, N, O, R, S, V, and Z). These letters are designed following the Snellen principle as well, however the Sloan letters have equal height and width (5x5) while the British Standard letters are in a 4x5 framework. These tests can be recorded in logarithm of minimum angle of resolution in minutes of arc (logMAR) and typically change by 0.1 logMAR each line, which means for each line the patient can read, the VA changes by 0.1 logMAR. It can also be recorded with by-letter scoring, which means that for every letter the patient can identify the VA changes by 0.02 logMAR.[13] The charts are typically marked with Snellen and logMAR notation. Snellen notation can be converted to LogMAR notation by taking the logarithm to the base 10 of the inversed Snellen fraction. For example, 6/60 would be equal to 1 logMAR. These charts are considered the gold standard for VA measurement and for use in research.

1.1.3.3 Snellen tumbling Es

This chart has only the letter E as designed by Snellen in four different orientations (up, down, left, right). The patient's task is to identify the direction of the bars of the letter, which makes the guessing rate 1 out of 4. The patient can point out the direction instead of naming it, giving this test the advantage that it can be used internationally in countries where Roman letters are not used. In addition, it is useful in adults, children, those with learning difficulties, and special needs populations who cannot read letters. On the other hand, when used in children, care must be taken as children often confuse right from left. An alternative approach is to have three options; up, down, or horizontal (so either right or left is accepted as a correct answers). In this case the chance level will be 1 out of 3.

1.1.3.4 Landolt C (broken wheel test)

This test follows a similar format to Snellen Es in the sense that it is one optotype repeated in different orientations. The optotype in this case is the letter C (or a broken ring), where the broken part could be up, down, right, or left.

In general, what differentiates these two tests (Snellen Tumbling Es and Landolt C) from symbol and letter charts is that the latter are heterogeneously designed. This means that there are differences among the optotypes i.e. they are not necessarily equally identifiable. This makes the Tumbling Es and Landolt C a more difficult task. On the other hand, both the tumbling Es and Landolt C have a higher probability of getting the correct answer by chance than letter charts.

1.1.4 Matching tests (pediatric optotypes)

Matching tests have been developed over the years to be used in children and special populations who cannot read letters. In a matching test, the patient is given a key card containing all optotypes or symbols used in the chart. The task is to find the optotype presented on the chart in the provided key card. A few of the most commonly used matching tests are listed in this section.

1.1.4.1 LEA symbols

This test uses four symbols: circle, square, house, and apple. These symbols are designed so that they would all blur equally. These symbols were not designed following Snellen principle, but instead they were validated on adult participants by altering the size to give the most similar results to Snellen Es.[14] Children can respond to this test by either naming the symbols or by matching.

1.1.4.2 Patti Pics

This test consists of 4 symbols: house, circle, apple, and square. The star was added later as a fifth symbol. This test was developed following the Snellen principle, meaning that the stroke width of the optotype is 1/5 of the whole optotype and subtends 1 minute of arc at the 6/6 level. It was tested and calibrated against gold standard ETDRs.[15] Both Patti Pics and LEA symbols are available in many formats; full chart, crowded single optotypes (using crowding bars), uncrowded single symbols, and with both tests the patient can name or match the optotypes.

1.1.4.3 Kay pics

This test was first designed to be used without a matching card and the patient would respond by naming the symbol. The symbols are more like pictures than the LEA or Patti Pics, so that it could be easier in a slightly younger age group. Eight pictures are included in this test: truck, apple, boot, clock, fish, cup, house, and duck. The idea behind the large number of optotypes is to make it more interesting. However, this could be a disadvantage since the task depends on the child's knowledge of these pictures. The optotypes in this test were designed to partially follow Snellen principle. The stroke width was made so that it subtends 1 minute of arc at the 6/6 level, but the stroke width is not 1/5 of the full optotype.[16] In fact, a 6/6 optotype for example is almost double the size of a Snellen letter. This is due to the complexity of Kay pics optotypes - they have more details than Patti Pics or LEA symbols. The details are made so that the shapes will make more sense to the child. A key card was developed later to introduce the child to the optotypes and to be used as a matching task, if necessary. Another issue with this test is that the pictures are not equally recognizable at threshold. For example, the duck is easier to recognize because of its overall shape than the truck or the boot. The Kay Pics company is currently restyling these pictures to make them more equally recognizable. Additionally, they tend to overestimate letter VA by 2 lines on average.[17]

1.1.5 Visual Acuity tests appropriate for use in infants 0 – 3 years old

There are different uses of the word "infant" in regards to age. It is sometimes used to describe the ages between 2 – 12 months. In this thesis, the term "infant" will be used to describe children from birth up to 5 years.

1.1.5.1 Fixation tests

An objective rough estimation about visual function can be obtained by these methods. In a child with strabismus, the fixation preference test is done by observing the fixation behavior of the eyes with the infant looking at a near target, and determining whether the patient prefers to fixate with one eye over the other or to alternate.[18] In children without strabismus, a vertical prism is used to force them to fixate with one or the other eye, but this test has been shown to have poor sensitivity.[18] Another method is called Central, Steady, and Maintained,[19] in which a grading system is used to record the accuracy of fixation. In another test, called preference for occlusion, when there is unequal acuity between the eyes the infant will be more resistant to occlusion of the good eye compared to the poorer eye. The validity of Central, Steady and Maintained and the preference for occlusion test have not been well studied.

1.1.5.2 Optokinetic nystagmus (OKN)

An OKN response can be elicited using a moving target (usually black and white grating) at a fixed speed in one direction. The movement produced by the eyes has two components: first a pursuit movement in the same direction as the moving grating; second, a saccadic movement in the opposite direction of the moving grating. Clinically, this test is usually performed using a cylindrical rotating drum (OKN drum) that is covered with alternating vertical black and white stripes, i.e. a square wave grating. The OKN test can be performed monocularly or binocularly, vertically or horizontally. The acuity threshold can be determined by decreasing the width of the stripes. Absent OKN response can indicate poor vision, while unequal responses between eyes or between vertical and horizontal movement can indicate a neurological lesion. In newborn babies, unequal monocular horizontal responses are normal (temporal to nasal > nasal to temporal). Temporal to nasal and nasal to temporal movements are found to be very similar in 5 months old and the difference is expected to completely disappear by 2 years of age.[20]

1.1.5.3 Visually evoked potentials (VEP)

The stimulus presented to the infant is usually a black and white checkerboard or square wave grating of decreasing size. The response is directly recorded, in the form of electrical activity, from the scalp using electrodes. The waveform of the responses that are synchronized with the visual stimulus are then analyzed using computer software. This method has an advantage of being an objective measurement that requires no active response from the infant. Sweep VEP is a fast way of measuring this in infants, in which a number of grating spatial frequencies are presented rapidly in succession during a few seconds.[21] Threshold is based on the significant responses above noise level and is calculated using variety of strategies.

1.1.5.4 Preferential looking tests

This method was introduced based on the infant's natural preference to look at a pattern rather than a blank area.[5] The forced choice preferential looking procedure is a psychophysical measurement which can be used for visual acuity measurement using a forced choice staircase method, but it takes a considerably long time to perform for clinical testing.[5]

1.1.5.4.1 Teller Acuity Cards

Teller et al.[22] were the first to transform preferential looking into a clinically applicable procedure to measure VA in infants that takes a few minutes to perform. This was called the acuity card procedure. This short testing time is crucial in testing infants because they have a short attention span and lose interest in the test very quickly. In the clinical setting, VA is only one component of a full eye examination so it cannot take up the entire attention span of the infant. This method yields good testability in this difficult to test age group (0 – 3 years).

The test consists of a set of cards with one card at each acuity level. The cards have a square wave grating on one side of the cards on a homogenous grey background that has luminance equal to the average of the black and white bars of the grating, so that at frequency levels that are above the resolution limit, the pattern looks like the homogenous grey background.[22] The test consists of 15 cards with grating size that ranges from 0.32 to 38.0 cycles per centimeter, (cpcm) in ½ octave steps (0.15 logMAR). A cycle consists of one black and one white strip and cpcm = cpd x testing distance/57). There is one grey card without gratings on either side, used to assess the infants looking behavior i.e. assess the infant's response to gratings above his/her threshold. Dimensions of the cards are 25.5 x 55.5 cm with a peephole in the middle of the card. The test is usually performed at 55 cm which enables testing VA from 0.31 to 26.0 cycles per degree or 20/1900 to 20/16 Snellen equivalent. The cards are also calibrated for various testing distances. The examiner holds the card and looks through the peephole to determine the direction of gaze of the infant while being blind to the position of the grating. After deciding the infant's response, the examiner looks at the card and checks whether it was correct. If the examiner was not sure of the infant's response, he/she can flip the card which should result in the opposite response and then decides if the infant can see the pattern or not. In the case of gratings above the infant's threshold, he/she will not look directly at either side of the card or will be equally interested in both sides of the card. The acuity is determined by the maximum spatial frequency which results in a clear, correct looking response. This test has been validated in infants and set as the gold-standard in the 0 – 12 months age group.

1.1.5.4.2 Cardiff Acuity Cards

This test follows the same general principles in card design and testing procedure as the Teller Acuity Cards. Woodhouse et al.[23] designed this test to be more interesting for toddlers (age 1 – 3 years old) by using pictures made of vanishing optotypes instead of square wave gratings. The vanishing optotypes have an overall fixed size schematic shape (car, train, duck, house, dog, and fish) where the outline of these shapes is a double black line separated by white line, so that the total luminance of the outline of the shape is equal to the luminance of the grey background. As the thickness of the lines decrease in visual angle, the shapes will be harder to detect. The cards are 28 cm long and 21 cm wide with the shape being either on the top or bottom of the card. This design was chosen because it is easier to detect vertical eye movements in the case of an infant with strabismus or nystagmus. The test is designed to be used at 0.5 m or 1m. At 1m it gives test values between 3.75 – 46 cpd (20/160 to 20/12.5 equivalent), but the distance can be adjusted to include more angular sizes.

1.1.6 Repeatability of VA charts and the agreement between them

Visual acuity values vary based on the measurement method. This may be because of the different levels of difficulty between the different tasks used in each test. Resolution acuity is often measured in cpd and optotype acuity (recognition) is often measured in logMAR or Snellen fraction. An adult with normal visual acuity may perform differently in different tests, but should demonstrate good VA on all tests. On the other hand, individuals with abnormal vision would show more discrepancy between tests. For example, Mayer et al.[24] compared resolution and recognition VA values in literate children, 27 months to 15 years. This study compared children with no visual anomalies, those with amblyopia, and those with foveal anomalies. The results showed that resolution VA over-estimates recognition acuity by 0.7 octave (0.21 logMAR) among all groups. Differences up to 1.5 octaves (0.45 logMAR) were recorded in the same study in patients with dense amblyopia and with foveal anomalies. The amblyopic group of this study showed mean differences between resolution and recognition VA of 1.08 octave (0.32 logMAR) while for the non-amblyopic group it was 0.4 octave (0.12 logMAR). These differences increased as recognition VA levels got worse for the amblyopic group while in the non-amblyopic group the differences remained constant. Drover et al.[25] studied children with amblyopia, at risk of amblyopia, and non-amblyopic children between the ages 3 to 18 years old. Each child was tested using Teller Acuity Cards and one of the following recognition acuity tests: crowded HOTV, crowded or a single line of: ETDRS letters; Lea symbols; or Snellen chart. The results overall showed higher resolution acuity levels than recognition with a mean difference of 0.46 logMAR (1.5 octave) and a median difference of 0.12 logMAR (0.4 octave). This difference decreased in cases of mild amblyopia and increased in severe cases (0.18 vs. 0.64 logMAR respectively). Similar results were shown by Moseley et al.[26] and Rydberg et al.[27] where the latter investigated more diverse groups, including: normal, visually impaired, and strabismic children and adults. The agreement between recognition and resolution acuities was higher when recognition acuity was measured using single optotypes than when measured using a line of optotypes.[27] The same pattern was found when Cardiff Acuity Cards (vanishing optotypes) were used for resolution acuity measurement (Cardiff Acuity Cards overestimate Bailey-Lovie by almost 2 lines).[28] The sensitivity of Cardiff Acuity Cards in detecting amblyopia was only 42%.[28] Kushner et al.[29] investigated the sensitivity of Teller Acuity Cards compared to Snellen chart in detecting different levels of vision deficits. This study found that Teller Acuity Cards have a sensitivity of 58% in detecting VAs of 20/40 (0.3 logMAR) or worse. This sensitivity decreases to 39% for VAs of 20/70 (0.5 logMAR) and decreased further to 24% for 20/200 (1 logMAR).[29] This means that in the presence of a normal resolution VA, a significant visual loss may still be found when recognition VA is measured. These studies demonstrate that in patients with amblyopia or foveal anomalies, recognition acuity is more sensitive than resolution acuity for detecting visual deficits. Thus, it is more useful in accurately detecting such conditions and monitoring the progress of treatment.

Optical blur also affects recognition and resolution acuities to different extents.[30] For example, +12D decreased Snellen acuity from 20/20 to 20/1000 while grating acuity was reduced to 20/80. This shows the effect of refractive error on VA even in the absence of any other ocular abnormalities.

The difficulty of each test, and the VA results obtained, also varies depending on optotype design or based on the task required of the patient. Bailey et al.[31] studied the variations between optotypes among ten different VA charts in normal adults under the same testing conditions and compared them to the gold standard ETDRS. LEA symbols and HOTV were the only tests which gave better VA than ETDRS with mean differences of 1 and 2 letters respectively (0.02 and 0.04 logMAR respectively). British Standard letters (Bailey-Lovie), tumbling Es, and Landolt C were all 1 letter worse than the ETDRS. Lastly, the Patti Pics symbols had a mean difference of 2 letters poorer than ETDRS. In conclusion, different tasks and test designs have significant impact in testing VA in adults or children.[24] A cognitively easy task may give a better VA value than another more challenging task, while the familiarity and difficulty of the optotypes may also affect recognition VA.[31]

1.1.7 Effects of crowding on visual acuity

Crowding is defined as the reduction of VA due to the nearby contours. This is due to contour interactions that fall within the same integration zone as the object in the higher visual areas in the visual cortex in the brain.[8] The object features are detected separately in the visual cortex (V1) and then analyzed in these integration zones to compose the whole object.[8] Crowding increases the difficulty of the recognition visual acuity task making it more sensitive for detecting visual anomalies.[32] Consequently resolution VA tests and interaction free recognition VA tests yield better VA levels than crowded recognition VA charts.[32] This effect has been shown to be more profound in amblyopic eyes.[33,34] For example, Gräf et al.[35] found that when testing amblyopic children and adults, VA using single Landolt Cs was two lines better than crowded Landolt Cs, while in normal eyes, the differences was 1.6 lines between crowded and single optotypes. This indicates the value of crowded recognition acuity testing in the detection and monitoring of amblyopia.

1.2 Development of Vision in Infants and Children

1.2.1 Development of VA

1.2.1.1 Babies aged 1 – 24 months

Visual acuity data for this age group is exclusively resolution VA. Values obtained using behavioral tests (subjective) from infants who are typically developed, free from ocular disease or abnormalities are displayed in Table 1.1[36–43] in six months steps. Age specifications and methods differ between articles, because the feasibility among the tests differ. For example, data for Cardiff Acuity Cards[43] are only available in infants aged 12 months or older. Similarly, articles studying resolution values usually do not include adult values, which makes determining the age when adult like levels are achieved inconclusive. Nonetheless, development trends can be obtained from these studies. From Table 1-1, we can conclude that newborns to 6 months of age have acuity of about 1 cpd (equivalent to 1.5 logMAR). This number increases rapidly during the first year of life to about 6 cpd by 12 months, although mean values up to 10 cpd in 12 month olds were reported by Courage et al.[40] During the second year of life, the development is slower, with values around 7 – 8 cpd at 18 months and 10 – 14 cpd at 24 months. Values obtained with the Cardiff Acuity Cards[43] (Table 1-2) are slightly higher than those obtained by Teller Acuity Cards.

Table 1-1. Age norms measured using gratings in PL (aged 0 – 24 months).

Age (months)	Binocular		Monocular	
	Mean Acuity and 95% CI		Mean Acuity and 95% CI	
	cpd	logMAR	cpd	logMAR
McDonald et al. (1985)[36]				
1	1.1 ± 1.1 oct	1.4 ± 0.33		
6	4.7 ± 0.8 oct	0.8 ± 0.24		
McDonald et al. (1986b)[37]				
1	0.8 ± 0.7 oct	1.57 ± 0.21	0.6 ± 0.7 oct	1.7 ± 0.21
6	5.3 ± 0.5 oct	0.75 ± 0.15	3.7 ± 0.9 oct	0.91 ± 0.27
12	6.3 ± 0.7 oct	0.67 ± 0.21	3.3 ± 0.9 oct	0.95 ± 0.27
McDonald et al. (1986a)[38]				
18	9.8 ± 0.4 oct	0.48 ± 0.12	7.3 ± 0.6 oct	0.61 ± 0.18
24	14.9 ± 0.6 oct	0.3 ± 0.18	13.2 ± 0.6 oct	0.35 ± 0.18
Mayer et al. (1995)[39]				
1			1	1.4
6			5.6 ± 0.5 oct	0.73 ± 0.15
12			6.42 ± 0.3 oct	0.67 ± 0.09
18			8.59 ± 0.4 oct	0.54 ± 0.12
24			9.57 ± 0.3 oct	0.5 ± 0.09
Courage et al. (1990)[40]				
1	1.1 ± 0.6 oct	1.4 ± 0.18		
6	5.9 ± 0.6 oct	0.7 ± 0.18		
12	9.6 ± 0.3 oct	0.5 ± 0.09		
18				
24	13.2 ± 0.5 oct	0.35 ± 0.15		
Harris et al. (1984)[41]				

1	1.3 (0.9 – 1.8)	1.36 (1.5 – 1.2)		
3	4 (2.8 – 5.6)	0.87 (1 – 0.7)		
5	5.2 (2.9 – 8.3)	0.76 (1 – 0.6)		
Leone et al. (2014)[42]				
6	6.33 (3.6 – 11.2)	0.67 (0.9 – 0.4)	5.72 (2.8 – 11.8)	0.72 (1 – 0.4)
9	6.43 (3.2 – 12.7)	0.66 (1 – 0.4)	5.58 (3 – 10.3)	0.73 (1 – 0.5)
12	6.74 (3.5 – 13.05)	0.65 (0.9 – 0.4)	5.98 (2.9 – 12.4)	0.7 (1 – 0.4)
15	7.34 (2.9 – 18.7)	0.6 (1 – 0.2)	6.56 (2.8 – 15.2)	0.66 (1 – 0.3)
18	7.57 (3.3 – 17.5)	0.59 (1 – 0.2)	7.54 (3.6 – 15.6)	0.6 (0.9 – 0.3)
21	9.02 (3.9 – 20.6)	0.52 (0.9 – 0.2)	7.37 (3.5 – 15.7)	0.6 (0.9 – 0.3)
24	10.96 (4.7 – 25.7)	0.44 (0.8 – 0.1)	10.71 (4.3 – 26.9)	0.45 (0.8 – 0.1)

CI = confidence interval, cpd = cycles per degree, oct = octave, grey cells denote data were not included.

Table 1-2. Age norms measured using Cardiff Acuity Cards (aged 0 - 24 months).

Age (months)	**Binocular**		**Monocular**	
	Mean Acuity and 95% CI		**Mean Acuity and 95% CI**	
	cpd	**logMAR**	**cpd**	**logMAR**
Adoh et al. (1994)[43]				
12	7.4 ± 0.53 oct	0.6 ± 0.16	7.6 ± 0.36 oct	0.6 ± 0.11
18	12.2 ± 0.43 oct	0.4 ± 0.13	10.8 ± 0.52 oct	0.44 ± 0.16
24	17.4 ± 0.38 oct	0.24 ± 0.11	15.2 ± 0.40 oct	0.3 ± 0.12

CI = confidence interval, cpd = cycles per degree, oct = octave, grey cells denote data were not included.

1.2.1.2 Infants 24 months – adult like

This age group has been more extensively studied than <24 months and includes resolution and recognition tests. This is because infants in this age can respond better to instructions and are more interested in these tests (pediatric optotypes), in addition to their increased cognitive abilities. Table 1-3 summarize studies of resolution visual acuity norms in this age group. Almoqbel et al.[7] and Stiers et al.[44] both included adult groups in their study. Almoqbel et al. found that adults have an average resolution acuity of 39.8 cpd, while Stiers et al. found mean resolution acuity of 50.4 cpd. Some differences in infant acuity levels between studies are found. For example, McDonald et al. and Stiers et al. showed binocular grating acuity of 27 – 30 cpd in 3 year olds,[38,44] while in other studies infants do not reach these values until 4 years of age.[39,45] These differences could be due to differences in study protocol or sampling.

Table 1-3. Mean and 95% confidence interval of resolution acuity values in infants aged 24 months and older.

Age (months)	**Binocular**		**Monocular**	
	Mean Acuity and 95% CI		**Mean Acuity and 95% CI**	
	cpd	**logMAR**	**cpd**	**logMAR**
Almoqbel et al. (2017)[7]				
72 – 84 (6 – 7Y)	31.6	-0.02		
96 – 108 (8 – 9 Y)	38	-0.1		
120 – 144 (10 – 12 Y)	38	-0.1		
Adults	**39.8**	-0.12		
Stiers et al. (2003)[44]				
33	28.9 ± 0.4 oct	0.02 ± 0.12		
39	32.5 ± 0.4 oct	-0.03 ± 0.12		

45	31.2 ± 0.4 oct	-0.02 ± 0.12		
51	33.8 ± 0.4 oct	-0.05 ± 0.12		
57	34.1 ± 0.5 oct	-0.05 ± 0.15		
63	36.9 ± 0.3 oct	-0.09± 0.09		
69	36 ± 0.4 oct	-0.08 ± 0.12		
Adults	**50.4 ± 0.23 oct**	**-0.22 ± 0.07**		
McDonald et al. (1986a)[38]				
30	23.4 ± 0.3 oct	0.1 ± 0.09	18.4 ± 0.5 oct	0.2 ± 0.15
36	27.7 ± 0.5 oct	0.03 ± 0.15	25.3 ± 0.5 oct	0.07 ± 0.15
Mayer et al. (1995)[39]				
30			11.52 ± 0.5 oct	0.4 ± 0.15
36			21.81 ± 0.4 oct	0.14 ± 0.12
42				
48			24.81 ± 0.3 oct	0.08 ± 0.09
Adoh et al. (1994)[43]				
30	21.9 ± 0.3 oct	0.14 ± 0.09	19.2 ± 0.3 oct	0.19 ± 0.09
Courage et al. (1990)[40]				
30				
36	18.6 ± 0.5 oct	0.02 ± 0.15		
42				
48				
Leone et al. (2014)[42]				
27	12.08 (4.5 – 32.2)	0.4 (0.8 – -0.03)	9.71 (3.8 – 25.1)	0.5 (0.9 – 0.08)
30	12.8 (4.5 – 36.2)	0.37 (0.8 – -0.08)	12.41 (4.3 – 35.4)	0.4 (0.8 – -0.07)
≥33	12.6 (5.5 – 28.7)	0.37 (0.7 – 0.02)	11.81 (5 – 27.7)	0.4 (0.8 – 0.03)

CI = confidence interval, cpd = cycles per degree, oct = octave, grey cells denote data were not included.

Normal values obtained using recognition acuity tests are only available using HOTV, Landolt C tests, and ETDRS, in infants aged 3 years or older (Table 1-4). In Stiers et al.,[44] using Landolt C as optotypes, infants aged 5 years 9 months (69 months) showed acuity of one line below adult levels (mean difference 0.1 logMAR) under binocular viewing. Atkinson et al.[45] showed that adult-like level of VA is achieved by 5 years of age (60 months) for single Cs, but only reach an acuity that is 58% of the adult threshold for crowded Cs. Using crowded HOTV, Drover et al. found that children reached monocular adult like levels of visual acuity at about 8 – 10 years.[46] When using the Bailey-Lovie chart, Almoqbel et al. found that children reached close to adult levels by 8-9 years.[7]

Table 1-4. Mean and 95% confidence interval of recognition acuity values in infants aged 24 months and older.

Almoqbel et al. (2017)[7]	**Crowded Bailey-Lovie**		**Uncrowded Bailey-Lovie**
Age (months)	**Mean Acuity (logMAR)**		**Mean Acuity (logMAR)**
72 – 84 (6 – 7Y)	0.012		0
96 – 108 (8 – 9 Y)	-0.04		-0.07
120 – 144 (10 – 12 Y)	-0.06		-0.08
Adults	**-0.1**		**-0.12**
Stiers et al. (2003)[44]	**Binocular Landolt C**		
Age (months)	**Mean Acuity and 95% CI**		
	cpd	**logMAR**	
33	37.7 ± 0.26 oct	0.26 ± 0.08	
39	40.3 ± 0.31 oct	-0.13 ± 0.09	
45	40 ± 0.37 oct	-0.12 ± 0.11	
51	45 ± 0.22 oct	-0.18 ± 0.06	
57	43.8 ± 0.42 oct	-0.16 ± 0.13	
63 (5Y 3 m)	48 ± 0.29 oct	-0.2 ± 0.09	
69	55 ± 0.33 oct	-0.26 ± 0.1	
Adults	**69 ± 0.16 oct**	**-0.36 ± 0.05**	

Drover et al. (2008)[46]	**HOTV w crowding bar**	
Age (months)	**Mean Acuity and 95% CI (logMAR)**	
36 (3Y)	0.08 (0.29 – -0.13)	
48 (4Y)	0.08 (0.25 – -0.09)	
60 (5Y)	0.03 (0.22 – -0.16)	
72 (6Y)	-0.03 (0.15 – -0.21)	
84 (7Y)	-0.02 (0.08 – -0.12)	
96 – 120 (8 - 10Y)	-0.06 (0.06 – -0.18)	
Adults	**-0.04 (0.13 – -0.21)**	
Leone et al. (2014)[42]	**HOTV w crowding bars**	**line ETDRS/HOTV**
Age (months)	**Mean Acuity and 95% CI (logMAR)**	**Mean Acuity and 95% CI (logMAR)**
<36	0.13 (0.11 – 0.15)	0.25 (0.20 – 0.30)
36 (3Y)	0.09 (0.07 – 0.10)	0.22 (0.17 – 0.26)
42	0.07 (0.05 – 0.09)	0.16 (0.14 – 0.18)
48 (4Y)	0.05 (0.03 – 0.06)	0.15 (0.12 – 0.18)
54	0.03 (0.02 – 0.04)	0.13 (0.11 – 0.14)
60 (5Y)	0.01 (0.00 – 0.03)	0.13 (0.11 – 0.14)
66	-0.01 (-0.02 – 0.00)	0.11 (0.10 – 0.12)
Dobson et al. (2009)[47]	**ETDRS**	
Age (months)	**Mean Acuity and 95% CI (logMAR)**	
60 (5Y)	0.16 (0.35 – -0.03)	
72 (6Y)	0.09 (0.24 – -0.06)	
84 (7Y)	0.06 (0.25 – -0.13)	
96 (8y)	0.03 (0.18 – -0.12)	
108 (9y)	-0.1 (0.05 – -0.25)	
120 (10y)	0.05 (0.42 – -0.32)	
132 (11y)	0.04 (0.29 – -0.21)	
240 (12y)	0 (0.35 – -0.35)	

CI = confidence interval, cpd = cycles per degree, oct = octave, grey cells denote data were not included.

1.2.2 Development of other aspects of vision

1.2.2.1 Contrast sensitivity

Contrast is defined as the relative difference in luminance between an object and its background. In case of stripes i.e. square wave gratings, Michelson Contrast is used.[48] It is calculated by the difference in luminance between the dark and light stripes divided by the sum of them. The threshold is then defined as the lowest contrast that a person can detect at a given size (spatial frequency). Contrast sensitivity (CS) is the reciprocal of the contrast threshold. Contrast sensitivity is often shown in a contrast sensitivity function (CSF), where contrast sensitivity is plotted against spatial frequency levels.[7] Normal adult CS for static gratings is decreased at low spatial frequencies (about 0.8 – 1 cpd). CS then increases as spatial frequency increases to the peak at about 4 cpd, after which CS starts to decrease as spatial frequency continues to increase.[49,50] This means that it is difficult to detect wide gratings and very thin gratings at low contrast, while intermediate gratings are the easiest to detect (1 – 4 cpd). The cut-off of sensitivity for 100% contrast at the highest spatial frequency is the limit of resolution VA.

Humans are born with very low contrast sensitivity for all spatial frequencies. CS increases very rapidly during the first few months of life across all spatial frequencies. Gwiazada et al.[51] show that mean CS at 2 months of age peaks at 0.3 cpd with values of 0.7 log units (20% contrast) and then decreases as spatial frequency increases to about 0.2 log units (63% contrast) at 1 cpd. As the child develops, the peak shifts to the higher spatial frequencies so that by the age of 6 – 8 months the peak is at 1 cpd with sensitivity of 0.8 log units (15% contrast). By the age of 4 years, the peak is close to adults at 3 cpd with sensitivity of 2.1 log units (0.8% contrast). Development continues at a slower pace until it reaches adult levels (approximately 2.5 log units, 0.3% contrast) after the age of 8 years.[51] Ellemberg et al.[52] found adult-like CS in children aged 7 years old and this study also showed that CS for higher frequencies tends to develop earlier than CS for lower frequencies. A review by Leat at al.[21] summarizes development of CS and it concludes adult sensitivity is reached between 8 – 10 years of age.

1.2.2.2 Visual field

Visual field (VF) is defined as the angular extent within which objects can be detected when the eyes are stationery. The normal adult monocular VF limit is 100° temporally from the central fixation point, 60° nasally, 65° above, and 75° below the fixation point. These values may vary because of obstruction by the surrounding structure of the face (nose in the nasal field and protruding orbital bone superiorly). The overall total binocular VF of normal adults is about 220° horizontally and there is about 80° of overlap between the two eyes.[49]

VF is measured in infants by moving an object from the periphery to the center, and observing the infant looking responses to the object. Once the infant responds to the presence of the object, it means that the object just entered the infant's VF. Schwartz et al.[53] examined infants 0 – 8 week old. They found that newborns have larger VF than both 4 and 8 weeks old. This unexpected finding is attributed to infant attention behavior. Infants of this age (4 and 8 weeks) are less likely to make a looking response away from the fixation target than newborns. In newborns, the vertical VF was more restricted than both horizontal and diagonal (25° vertically, 40° horizontally and diagonally). At the age of 4 weeks the visual field decreased to about 25° horizontally, 20° diagonally, and 15° vertically. By the age of 8 weeks the horizontal VF expands to about 40°, but the other meridians were almost unchanged. These values were significantly smaller than adults, but the VF shape was very similar to that in adults.

Mohn et al.[54] show a rapid increase in VF between the ages 2 – 8 months then slowed, the VF was still not adult-like by the age of 1 year (50°). In Quinn et al.'s study[55] by 4 – 10 years the VF was still expanding horizontally.

This VF development is strongly associated with retinal changes. Photoreceptors near the fovea move inward, which is associated with increased VA. Other retinal cells are known to move outwards from the center (macula) towards the periphery. This change is rapid during the first 3 months of life, after which it continues at a very slow rate to about 1 year of age.[49] Other features of the retina such as the fovea continue to develop beyond this time e.g. foveal thinning.

1.2.3 Development of refractive error

Current literature studying refractive error is based on cycloplegic and non-cycloplegic refraction. In the pediatric population, it is essential that cycloplegic objective refraction is performed to eliminate accommodation. This is done by installing cycloplegic drops into the patient's eyes before the measurement. The cycloplegic agents in these drops temporarily paralyze the ciliary muscles that are responsible for accommodation. This is the most effective way to control accommodation. Other methods to control accommodation in infant and children include the use of fogging lenses or near retinoscopy (Mohendra technique). It was found that near retinoscopy gives significantly less hyperopic refraction in infants compared to cycloplegic retinoscopy.[56]

In the first year of life, most studies show that refractive errors are higher than in adulthood, and they decrease during the first few years of life. This is called emmetropization, which is defined as the change from ametropia to emmetropia which occurs during development so that the axial length of the eye changes to matches the focal length of the optical system of the eye.[57]

In a population-based study using cycloplegic retinoscopy, Mayer et al.[58] showed that the emmetropization of hyperopia is very fast during the first 6 months of age and slows down with age. Over this time period the average spherical equivalent (SE) decreases from hyperopia towards emmetropia. In addition, the width of the refractive error distribution decreases (smaller SD). After about 6 years of age, the width of the distribution then increases again due to the onset of myopia.[59] Zadnik et al.[60] studied school-aged children between 5 – 12 years old using non-cycloplegic refraction, and found that emmetropization of the hyperopes continued in this age group but at a considerably slower rate, with an overall decrease in SE of only 0.23 Diopters (D) from 6 to 12 years. Larsen[61] agrees with both studies and showed that mean SE reached 0 D (emmetropia) around 12 years of age, based on findings using cycloplegic refraction. In a non-cycloplegic retrospective population-based study, Irving et al.[59] showed that the most hyperopia (mean SE of +1.79 D) is found between 0 – 12 months. The mean refraction then decreased, with emmetropization continuing to occur on average until around 9 years. The Multi-Ethnic Pediatric Eye Disease Study[62] showed that there are ethnic differences in the prevalence and development of refractive error. This study measured cycloplegic refraction and showed that the mean SE between 6 – 72 months was around +1 D. The SE did not significantly change among this age group, although there was a shift in the distribution (to around 3 years of age) towards the mean (smaller SD).[62] The prevalence of hyperopia decreased in 0 – 6 years age group as well, indicating the emmetropization of hyperopia.[62] The prevalence of myopia also decreased in this age group, indicating that myopia in infants does emmetropize and the onset of myopia generally does not occur again before 6 years of age.

Astigmatism of 1D or more has a high prevalence in the first year of life and decreases significantly in the first few years of life.[58,63] The age at which astigmatism stabilizes and becomes adult-like is still debatable. Mayer et al. found this to occur at 18 months of age.[58] In their study, with the rule astigmatism was more prevalent in newborns (1 – 1.5 months), while against the rule astigmatism was more prevalent in all other age groups (2.5 – 48 months).[58] Some studies show that oblique astigmatism was relatively unchanged throughout the years,[64] but most show it decreases.[58] However, Irving et al. found that average astigmatism was 0.5 D in infants 0 – 12 months, and that it gradually increased with age[59] – this is not typically found in other studies. Mean SE from 1 month – 13 years is shown in Table 1-5.

Table 1-5. Development of mean and confidence interval of spherical equivalent in newborns until emmetropization.

MEPED (2010)[62]	**African American**		**Hispanic**	
Age in months (years)	Mean SE (D)	95% CI (D)	Mean SE (D)	95% CI (D)
6	0.6	3.34 − -2.14	1.29	4.03 − -1.45
12 (1y)	0.7	3.25 − -1.85	1	3.94 − -1.94
24 (2y)	0.9	3.45 − -1.65	1.1	3.84 − -1.64
36 (3y)	1.1	3.84 − -1.64	1.3	4.04 − -1.44
48 (4y)	1.1	3.84 − -1.64	1.4	3.95 − -1.15
60 − 72 (5 – 6y)	1	3.55 − -1.55	1.35	3.70 − -1.00
Mayer et al. (2001)[58]				
Age in months (years)	Mean SE (D)	95% CI (D)		
1	2.2	5.51 − -1.12		
6	1.79	4.39 − -0.81		
12 (1y)	1.57	3.16 − -0.01		
18	1.23	3.09 − -0.64		
24 (2y)	1.19	2.89 − -0.50		
30	1.25	3.07 − -0.57		
36 (3y)	1	2.56 − -0.56		
48 (4y)	1.13	2.89 − -0.62		
Zadnik et al. (1993)[60]				
Age (years)	Mean SE (D)	SD (D)		
5	0.71	0.68		
6	0.73	0.87		
7	0.71	0.62		
8	0.37	0.89		
9	0.37	0.84		
10	0.23	1.69		
11	0.3	1.34		
12	0.5	0.43		

Larsen (1971)[61]		
Age (years)	Mean SE (D)	SD (D)
1	1.51	1.26
2	1.22	1.29
3	0.86	1.1
4	0.51	0.79
5	0.67	1
6	0.62	1.32
7	0.61	1.22
8	0.6	1.15
9	0.48	0.78
10	0.69	1.28
11	0.65	1.13
12	0	0.63
13	0.08	0.6

SE = spherical equivalent, D = diopter, CI = confidence interval, SD = standard deviation, grey cells denote data were not included.

1.2.4 Development of eye movements

1) Smooth pursuit is a voluntary version eye movement (when both eyes move together in a conjugate fashion in the same direction). It occurs to localize the image of a moderately to slowly moving target on the fovea in order to produce a sharp image. In adults with normal vison, the speed of pursuit movement ranges between 0.08 to 40 degrees/sec. Newborns can only follow very slow objects (5-15 degrees/sec). Smooth pursuit develops rapidly within the first 4 months of life to about 32 degrees/sec,[49,65] but it is not an entirely smooth movement. Quick saccadic movements occur which allow the eyes to catch up to the target. Adult-like movement is not achieved until late teens.[49,66]

2) Saccades are voluntary version fast movements that occur to catch up with a fast-moving stimulus or to move between static objects, in order to keep the image of the object of interest on the fovea. Adult eyes can perform a saccadic movement up to 600 degrees/sec at a latency of 0.2 seconds.[67] Newborns also have the ability to perform saccades but are not as accurate or as fast. They usually undershoot and need to perform more than one saccadic movement to arrive at the target.[68] In addition, the latency of response is about 0.5 seconds, as well as the time spent to perform the additional saccadic movements (total 2 seconds).[49] The latency of saccades reach maturity after the age of 18 years.[69,70] As the infants get older their ability to perform accurate saccadic movement increases rapidly in the first year of life, [71] but adolescents still make errors (undershoot/overshoot). These errors depend on step size.[72,73] Adult-like saccadic movements were reported by about 12 years of age.[73]

3) The vestibulo-ocular reflex (VOR) is an involuntary movement that occurs as a reflex to head movement to maintain foveal fixation of the target. The movement is initiated by the semi-circular canals in the middle ear, in approximately equal magnitude and opposite direction of the head movement as fast as 0.016 seconds after head movement in normal adults.[49] This pattern of reflex eye movements is found to be more developed in normal full-term newborns than in adults for rotation in the dark, and equal to adults when a background stimulus is used.[74]

4) Optokinetic response is an involuntary movement that occurs in response to a moving visual field in one direction to maintain the foveal fixation of the object. It consists of a smooth movement in the direction of the stimulus that is usually followed by a saccadic movement in the opposite direction as a reset when the limit of the eye movement is reached. An example of the use of this reflex to judge VA has been described in 1.1.5.2. Optokinetic response is present in infants, but it does depend on their ability to see the target, meaning that their response can only occur when the target is above their VA threshold. OKN responses are slower than adults. In addition, there is an asymmetry in horizontal monocular responses (temporal to nasal > nasal to temporal) usually found in infants younger than 5 months of age (see 1.1.5.2).

5) Vergence movement is when the eyes move in opposite directions (disjunctive), either inwards (convergence) or outwards (divergence) to maintain both eyes on the object of regard. Newborns do not accurately maintain bi-foveal fixation because the fovea is not fully developed at this age and VA is poor. It has been shown that by 1 month of age infants can perform vergence movements in response to moving targets, and by 3 months of age most can respond to the introduction of a disparity (20Δ test).[75] Candy et al. found that even 5 week old infants can perform vergence movements in response to differences in stimulus.[76]

1.2.5 Preference for faces

Infants show a strong preference for looking at faces compared to other objects. Studies in the psychology literature usually utilize schematic drawings of faces to test whether infants prefer to look at face stimuli compared to non-face stimuli.[77–82] These studies often use the same features of the face stimuli and scrambled them so that the scrambled face will serve as the non-face stimulus and will have total luminance equal to the face stimulus. One interesting study[80] has shown that there is even a significant difference between newborns' (mean age 9 minutes) following responses to moving face stimuli and scrambled faces stimuli. There was also a preference for face stimuli compared to blank targets without any previous exposure to any faces. Another study by Maurer and Barrera[81] showed that the preference to look at faces is significantly stronger than the preference to look at scramble faces by 2 months of age, but not at 1 month of age. Other studies also agree with Maurer and Barrera and indicate the older the infant the stronger the response, and older infants responded more strongly when there were more details and features to make the faces "more realistic".[78,79] These preferences are not exclusive to schematic faces but also include face photographs[82] and animated faces in videos[78] in a complex background or surrounded pictures.

Schematic faces have been successfully used in the form of a vanishing optotype (see 1.1.5.4.2) to measure resolution VA in preferential looking format in infants aged 1, 3, and 5 months. In this case, the preferential choice was between the face on one side and no stimulus on the other side. This was compared to gratings.[41] Alternatively, face compared to a non-face vanishing optotypes in a preferential looking format could only be used at the age of 18 months upwards due to the complexity of the test. In this case the infant had to choose the face when presented with two vanishing optotypes on each card.[83]

1.3 Infants attention and behavioral changes

Infants' development is important to optometrists. Specific information about each child's behavior must be obtained, to choose the appropriate test with the appropriate level of difficulty. The optometrist's observation, in addition to the parental report, of the child's development is critical in detecting any systemic disease or developmental delay that may affect the child's visual functions. There are general age-related developmental milestones for infants, although normal variability should be considered and each infant will develop at a slightly different rate. Delay in development of a certain skill does not necessarily mean that the child is "abnormal".[84]

As shown in a previous section (1.1.5.4), newborns can detect and look at patterns and faces from a very young age, in addition to differentiation of sounds. The newborn's world is small and their range of attention is limited. As the infant grows in their first year their attention increases to include their hands and legs first (4 months) and then surrounding objects until about 12 months. At this stage the size of their world increases, as well as their verbal abilities.[49] Development of their behavioral responses continues after 1 year of age. Before that their responses were in form of looks, head-turn or smiles, but between 1 – 2 years they start to respond verbally or by pointing. Ciner et al.[85] showed in a stereo acuity study that infants 6 – 18 months could not be tested using pointing responses, while in 19 months old and older pointing responses were effective (passing criteria was 6 correct responses out of 8). Between 2 – 3 years (pre-school age), they are able to respond to more complex tasks e.g. match shapes or colors. Hence their ability to do a matching VA task. By 4 – 5 years, or once they become familiar with numbers and letters, they would be able to match letters even before they completely learn their alphabet. Ciner et al.[86] compared testability of matching HOTV test to matching LEA symbols in 30 – 36 months age group. The testability percentage was 71% and 75% for HOTV and LEA respectively. The HOTV test was found to be easier than the matching ETDRS since there are only 4 options in the HOTV. Success rate in 5 year olds was 52% and 100% when doing matching ETDRS and HOTV, respectively.[87] This makes the HOTV more similar to matching symbols than matching letters. Another study[88] showed that 100% of children between 5 – 7 years can perform a 7-option letter matching test and full Tumbling Es chart, while only 82% could perform the Snellen full letter chart. In the younger age group (3 – 5 years), 95% could perform 7-option matching letter test but only 62% could perform matching Tumbling Es. This is expected since children in this age are often confused by the directions (right vs left). As children start school, they start to understand complex commands and respond with full correct sentences and testing using a letter chart is possible. These findings indicate the need to measure recognition acuity in younger children and ideally children of all ages using a test that is comparable to the adult gold standard.

Chapter 2- Purpose and Hypotheses

2.1 Importance

The ultimate purpose of this work was to develop a visual acuity test to measure recognition acuity at a younger age than is currently clinically possible. Recognition VA currently is only testable in children aged 3 years or older[27,89,90] and it is only possible to reliably measure resolution (grating) VA in children below this age. Resolution VA is less sensitive in detecting visual anomalies especially those affecting central VA i.e. the fovea. On the other hand, recognition VA yields more sensitivity and is considered the gold standard for detecting and monitoring reduced VA. In addition, the use of the crowding phenomenon can be applied to recognition VA tests, but not those that employ resolution acuity targets.

The concept behind this study was to utilize the infants' natural preference for faces and construct schematic face optotypes to be used in a test of recognition acuity suitable for infants. The infants are expected to prefer to look at these face optotypes when presented next to a non-face target. It is important that the design of these optotypes follow Snellen principles in the size of each detail of the targets so that it subtends 1 minute of arc for the 6/6 size and to make both the optotypes of equal legibility at every size.

2.2 Study design

2.2.1 Preliminary studies

The first task was to develop targets that followed the Snellen principle, but which also had a face-like appearance and an alternative non-face target which would be equally discriminable at the acuity threshold. Firstly, several versions of the schematic face optotypes were designed and tested on adult participants to choose the optimal version of the optotype to be used in the main experiment. This part of the study was in collaboration with Darren Gigliozzi, a summer student in Dr. Leat's and Dr. Irving's lab.

Secondly, in babies aged 3 – 15 months, the strength of the preference for looking at schematic faces compared to similar non-face optotypes was tested. The optotypes used were the optimum face targets from the previous adult experiment. The optotypes were presented in a two alternative forced choice format.

2.2.2 Main studies

Two recognition acuity tests were developed (Face Cards and Patti Pics Cards) and validated against the gold standard optotypes in adult participants (ETDRS) (validation study). In the infant experiment, I tested the feasibility of: 1) using simple schematic smiley faces as optotypes in a two alternative forced choice preferential looking (2AFC) format (Face Cards) to measure recognition acuity in infants aged 16 – 42 months. 2) compared to Patti Pics symbols[15] presented in the same format. The development of recognition acuity using these two tests was observed in the same sample, in comparison with the development of VA measured with the Cardiff cards, a test of resolution acuity which is the gold standard for testing VA in this age group.

Both studies were cross-sectional studies for infants and adults, with the use of optical blur in adults to stimulate different levels of VA.

2.3 Hypotheses

- Face Cards and Patti Pics in a 2AFC format give equivalent VA to ETDRS in adult participants.

- Recognition visual acuity is measurable using looking or pointing responses in a 2AFC format at a younger age than is measurable with matching.

- Face targets have better testability than Patti Pics symbols in infants aged 16 to 42 months.

- Testability of Face Cards and the Patti Pics Cards increases over the age range of 16 to 42 months.

Chapter 3- Preliminary Studies

3.1 Testing face targets on adults

3.1.1 Introduction

The purpose of this investigative study was to compare different variations of face targets, to determine the face/non-face combination and characteristics that would give the most similar visual acuity measurement (VA) to the gold standard ETDRS and Snellen tumbling Es in adults. It is intended that the final face target will be used as an optotype to develop a test of form VA in infants.

3.1.2 Methods

A total of 55 adult participants were asked to identify each of five optotypes presented together in a line. Each participant was asked to identify several different sets of optotypes. The number of participants in each trial is shown in Table 3.1. First, a set of face targets in five different formats were presented; happy, sad, upside-down, scrambled and neutral as shown in Figure 3-1. These targets were constructed based on Snellen principles, where the detail of the optotype is 1/5 of the whole optotype and subtends 1 minute of arc at the 6/6 (0.0 logMAR) level.

Figure 3-1. Simple face targets with thick border.

Second, a single line consisting of five letters of the ETDRS chart was presented on a digital projector (ProVideo Classic, Inovva Systems). Lastly, a line of five Snellen tumbling Es in different orientations was used. Each line of targets was presented once. Each set of targets was presented in 15M and 3M letter size (equivalent to 6/15 and 6/3 at 6 meters or 20/50 and 20/10 at 20 ft). The participants viewed the 15M targets while wearing a +2D blurring lenses over their full distance correction and viewed the 3M targets while wearing their full distance spectacle correction. The maximum distance where the subjects could correctly identify at least three out of five targets was recorded. Visual acuity measurements were converted to logMAR notation. Mean VA for every variation of the face target was compared to the mean VA of either ETDRS letters or Tumbling Es (Tumbling Es were only used in case of face target in different orientations).

The face targets were tested and successively modified in six trials to obtain the optimal agreement in comparison to ETDRS and Snellen Tumbling Es. Based on the results of the preceding trials, we varied the parameters in the following ways.

3.1.3 Trial 1

A simple face with a thick border and a complex face with the same thick border were tested against the ETDRS (Figure 3-1 and Figure 3-2). These targets were previously designed by A. Hathibelagal. These face targets did not exactly follow the Snellen principal, as the spacing between the details was not equal to the width of the details. Although the lines were 1/5 of the whole optotype, the spacing between lines was larger. This trial showed that both these versions of simple and complex faces were harder to identify than ETDRS letters (see Table 3-1) i.e. visual acuity was poorer. As the complex face had more elements and thus was more difficult to manipulate and maintain the Snellen principles, the simple face was chosen for the second trial.

Figure 3-2. Complex face with thick border.

3.1.4 Trial 2

Since the borders may be contributing an amount of crowding, the simple face was tested with two different border options, a thin border (2 points) (Figure 3-3 a) and no border (Figure 3-3 b). Both versions gave better VA than ETDRS letters. It was noted that the thin border was not visible at the threshold level, so may not have been contributing to the visual acuity result.

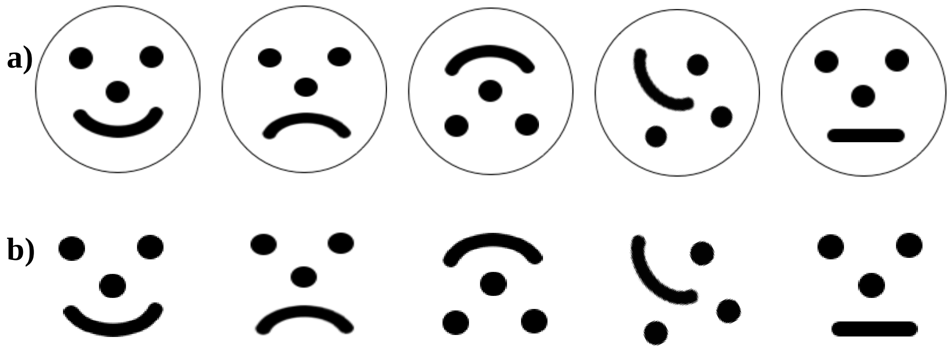


Figure 3-3. a) Simple face with thin border (2 pts). b) Simple face with no border.

3.1.5 Trial 3

Since faces in trial 2 were slightly easier than ETDRS, the border thickness was increased by 0.5 points to 2.5 points to test a medium border thickness in this trial (Figure 3-4). This face optotype was more difficult to identify than ETDRS letters (mean difference -0.12 logMAR). It seems that the border width is a determining factor in the equivalence to ETDRS acuity.

Figure 3-4. Simple face with medium border thickness (2.5 pts).

3.1.6 Trial 4

An oval simple and complex face with border thicknesses of 2.5 were tested. (Figure 3-5). Both simple and complex oval faces were more difficult to identify than ETDRS letters (mean difference of -0.14 and -0.12 logMAR respectively). This result was similar to the round face of the same border thickness (Trial 3), so the oval faces were discarded.

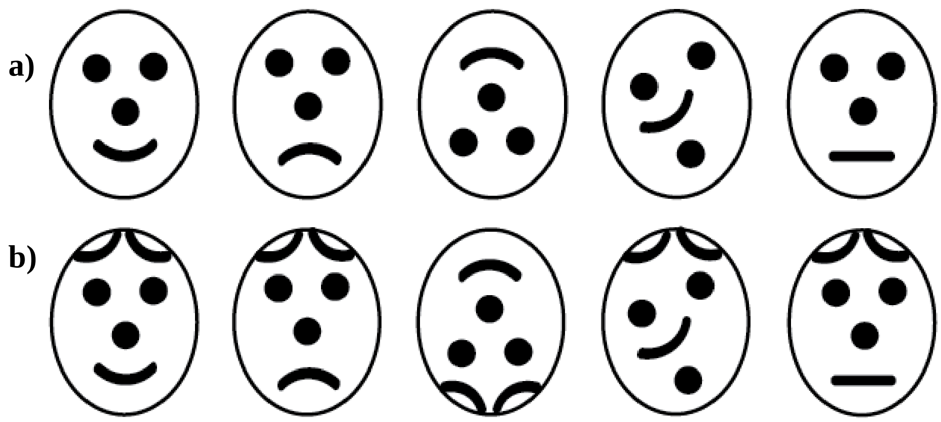


Figure 3-5. a) Oval simple face b) Oval complex face.

3.1.7 Trial 5

This tested two different border thicknesses, 2.5 and 2.1 points, and with only four variations of the face target; happy, sad, upside-down, and scrambled. The purpose of the 4 target versions was to compare more accurately with Tumbling Es, which have 4 possible responses. One of these options was repeated to make five targets in a line. An example of this presentation with the 2.1 point border thickness is illustrated in Figure 3-6, while the faces with 2.5 point border thickness are shown in Figure 3-4. The 2.5 point border gave very similar VA to Tumbling Es while the 2.1 border gave VA that was nearly 2 lines better than Tumbling Es.

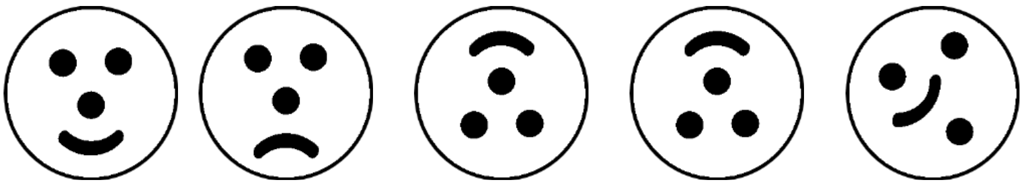


Figure 3-6. Simple face with 2.1 thickness border.

3.1.8 Trial 6

The simple smiley face with 2.5 point border thickness was tested in four different orientations (Figure 3-7) and compared to Tumbling Es. The face targets were 4 lines worse than the Tumbling Es. The results of these trials are shown in Table 3-1.

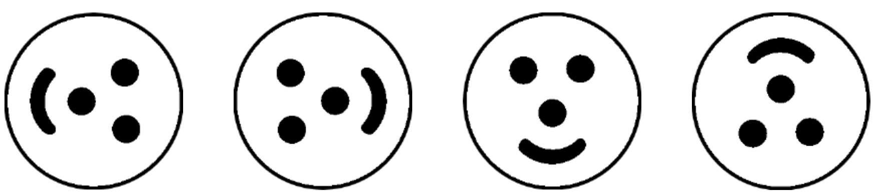


Figure 3-7. Simple smiley face in different orientations.

Table 3-1. Summary of the mean difference between face targets and ETDRS letters or tumbling Es.

Trial	**Number of participants**	**Condition**	**Mean difference between faces and ETDRS**
1	10	Thick border simple face Thick border complex face	-0.21 logMAR -0.17 logMAR
2	16	Thin border (2 pts) simple face No border simple face	0.05 logMAR 0.08 logMAR
3	8	Modified border (2.5 pts) simple face	-0.12 logMAR
4	10	Simple oval face Complex oval face	-0.14 logMAR -0.12 logMAR
Trial	**Number of participants**	**Condition**	**Mean difference between faces and Tumbling Es**
5	5	Modified border (2.5 pts) simple face Thin border simple face (2.1 pts)	-0.04 logMAR 0.19 logMAR
6	6	Modified border (2.5 pts) simple face in different orientations	-0.41 logMAR

3.1.9 Discussion and conclusion

The final target chosen to go forward with for creating the face targets for infant VA testing was the simple smiley face with a 2.5 point border thickness. These face targets gave a mean difference of 0.12 logMAR compared to ETDRS (about one logMAR line better than ETDRS), which could be caused by differences in guessing rates between the two tests since there are only five different variations for the face set and ten letters in the ETDRS chart. Although the thin border and no border gave closer results (underestimating VA by 0.05 and 0.08 logMAR respectively), the no border option was not very face-like to adult observers. The border of the face seems to be important to make the optotype more representative of real faces and thus more interesting to the infants. The thinner border (2 pts) was not identifiable at threshold, and therefore is not expected to influence the VA. The scrambled face and a dotted target (Figure 3-8) were chosen to be presented with the smiley face when tested on infants in two alternative forced choice format. These targets were chosen because they do not make sense as face targets but have similar feature/line contents to the face and can be used to create targets based on the Snellen principles.

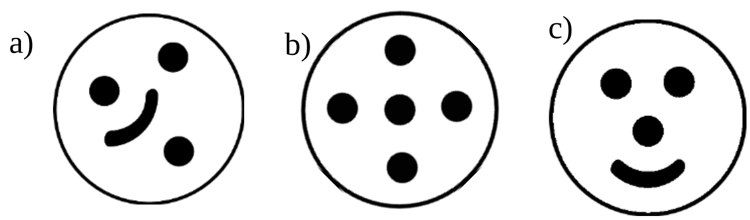


Figure 3-8. a) Scrambled face b) Dotted target c) Simple smiley face.

3.2 Testing face targets on infants

3.2.1 Introduction

The purpose of this study was to measure the strength and duration of the preference for faces compared to a non-face target, in order to determine the potential of measuring recognition VA in infants based on a preferential look for faces. The face targets were presented in a two alternative forced choice format (2AFC), with either of the two different non-face targets: the scrambled face or the dotted target (Figure 3-8). The targets were chosen based on the results of the previous experiment. This experiment also compared the testability of these targets using two methods of presentation, the non-contact gaze tracker and preferential looking cards.

3.2.2 Phase 1

3.2.2.1 Methods

3.2.2.1.1 Gaze tracker

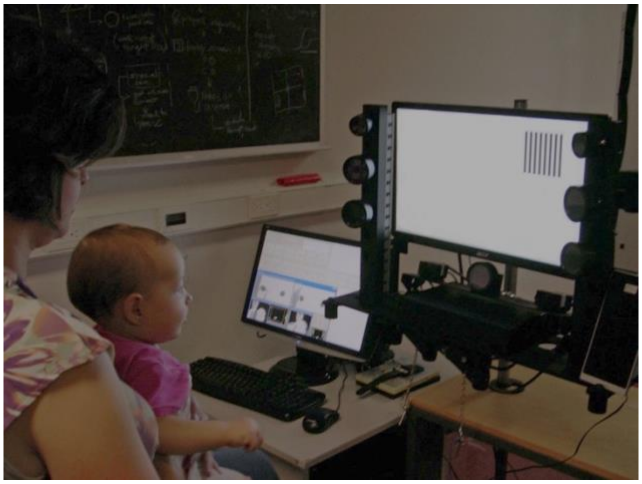


Figure 3-9. An infant participant viewing the non-contact gaze tracker.

The non-contact gaze tracker shown in Figure 3-9 is run using eye tracker software installed on a desktop computer. It consists of two monitors, one which serves as the operator monitor and one as the subject monitor (to display the targets). There are seven infrared lights which are positioned around the subject monitor, three on either side of the monitor and one below. Two commercially-available video cameras are positioned below the subject monitor. The software analyzes the eye features (pupil center and corneal reflexes) from the input of the video cameras to calculate the optical axis and the angle between the visual and optical axes (angle kappa) of both eyes as references to estimate the position of gaze.[91] A quick probabilistic calibration is based on the fact that infants are more likely to fixate on a target rather than a homogenous area. This approach does not require continuous fixation, which makes it useful in infants.[92] During calibration, clusters of fixation points from the infant as a response to cartoon images are used to determine the point of gaze. During the presentations, live tracking of each eye is represented on the operating monitor by a cluster of dots in a different color for each eye.

The targets were arranged in video sequences. Each video consisted of 15 target presentations with dynamic cartoon fixation targets in between, to bring the infants' attention to the center of the screen. Each target presentation consisted of a simple face next to a non-face in 50M (equivalent to 6/500) size positioned side by side in the middle of the screen for a few seconds (Figure 3-10). The position of the face was randomly assigned to the right or the left. Then the targets separated at 3.7 cm/sec to either side of the screen where the total separation is 26 cm (Figure 3-11). The speed was chosen to be slow to prevent the task from becoming a dynamic VA measurement, and slow enough that infants can easily follow.[65]

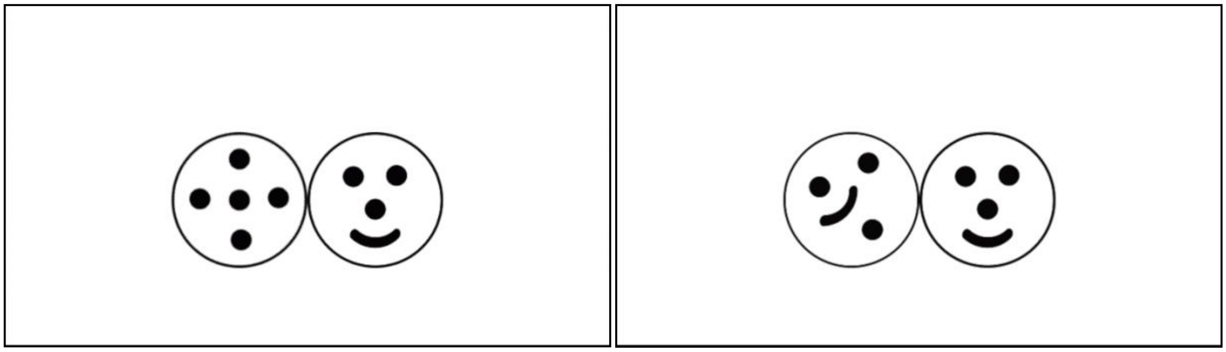


Figure 3-10. Face target vs dotted-target and face target vs scrambled face as they first appear in the gaze tracker videos.

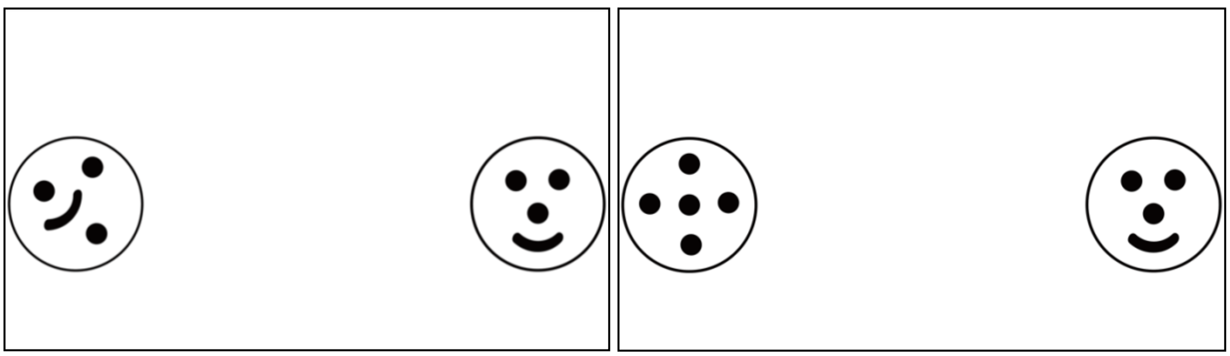


Figure 3-11. Face target vs dotted-target and face target vs scrambled face with maximum separation as shown in the gaze tracker videos.

3.2.2.1.2 Preferential looking cards

Each card had a simple face and a non-face target. The cards were designed so that the targets presented had the same dimensions and separation as presented in the gaze tracker. The overall dimensions of the cards were similar to those of the Teller Acuity Cards, 75cm x 56cm, with a peephole in the middle to observe the direction of gaze of the participant. The cards were presented in a random order.

3.2.2.1.3 Participants

We recruited healthy and normally developing infants, aged 3 to 15 months, without any reported significant ocular health problems (e.g. no strabismus); gestational age between 37 and 42 weeks at birth; normal development and general health as reported by parents. Normal visual development was measured and visual acuity[37,43] and refractive error[63] should be within normal limits for their age, as illustrated in Tables 3-2, 3-3 and 3-4. Participants were recruited from the School of Optometry and Vision Science clinic records and by flyers in the waiting areas of the clinics, in addition to the bulletin boards in Bright Start's daycare. Informed consent was obtained from the parent or guardian prior to the testing.

Table 3-2. Binocular upper and lower 90% limits for Teller Acuity Cards modified from McDonald et al 1986a.[38]

Age (months)	**Normal Binocular Acuity by Teller Acuity Cards**		
	Cycle per degree	Snellen equivalent (meter)	logMAR
4 – <6	2.0 – 6.2	6/96 – 6/30	1.2 – 0.7
6 – <12	2.6 – 12.0	20/76 – 6/15	1.1 – 0.4
12 - <18	2.6 – 12.0	20/76 – 6/15	1.1 – 0.4
18 – 24	5.0 – 18.0	6/38 – 6/9	0.8 – 0.2

Table 3-3. Binocular upper and lower 95% limits for Cardiff Acuity Cards modified from Adoh and Woodhouse 1994.[43]

Age (months)	**Normal Binocular Acuity by Cardiff Acuity Cards**		
	Cycle per degree	Snellen equivalent (meter)	logMAR
12 – <18	15 – 3.7	6/12 – 6/50	0.3 – 0.9
18 – <24	23 – 7.5	6/8 – 6/27	0.1 – 0.6

24 – <30	30 – 9.4	6/6 – 6/18	0.0 – 0.5
30 – 36	33 – 15	6/5.5 – 6/12	-0.05 – 0.3

Table 3-4. Cut off limits for refractive error according to age.

Age (months)	**Refractive error**			
	Hyperopia	Myopia	Astigmatism	Anisometropia
<6	< 4D	< 2D (1D when measured by cycloplegic refraction)	< 2D	< 1D
6 – 12	< 3D (3.5D when measured by cycloplegic refraction)	< 1.5D (1D when measured by cycloplegic refraction)	< 2D	< 1D
12 – 21	< 2.5D	< 1D	< 2D	< 1D

3.2.2.1.4 Screening for eligibility

The following tests were done to determine normal visual development of the participants. All tests were done under binocular viewing. At the first visit, ocular alignment was assessed by Hirschberg and cover test using the thumb as an occluder and a finger puppet as a target. Ocular motility was assessed using finger puppets. The following tests were divided between the visits and spread through each visit instead of prior to testing as usually done, in order to not fatigue the infants. The Infant's refraction was measured using retinoscopy with lens bars and one of the following techniques depending on the infant's age: 1) Distant static retinoscopy with +2D pediatric blurring glasses and a TV with a cartoon playing as a distant viewing target to relax the infant's accommodation; 2) Mohindra technique, performed in a completely dark room at 50 cm viewing distance and subtracting 0.75DS from the final spherical result.[56] Resolution acuity levels were obtained by Teller acuity cards for infants younger than 18 months[22] and Cardiff acuity cards for infants older than 18 months.[23]

3.2.2.1.5 Testing procedure

Each participant made two visits to the School of Optometry and Vision Science, no longer than 1 week apart. This was done to test each face/non-face combination in a separate visit, to avoid fatigue. The order of testing was alternated between the two combinations for each participant. For example, participant 1 viewed the face/dotted-target at the first visit and face/scrambled face at the second whereas participant 2 viewed the face/scrambled face at the first visit and face/dotted-target at the second. The participant was seated on their parent's/guardian's lap, 60 cm away from the target (monitor or card). Testing was done binocularly for all presentation methods and sequences. Ten successful looking responses were obtained and analyzed for each sequence.

3.2.2.2 Results

Eight infants were tested, median age 10.5 (range 8.5 – 14 months). With the gaze tracker, the percentage of correct looks was 53% and 62% for faces when presented with scrambled faces and dots respectively. For the cards, these percentages were 55 and 51% respectively.

3.2.3 Phase 2 (Habituation)

This experiment was introduced because the face targets did not result in a sufficiently strong looking responses from the infants. The concept is to familiarize the infants to the non-face target so that they will spend less time visually exploring it, and will be more inclined to look at the face if they see it.[93] This concept of habituation has been successfully used in previous infant experiments.[94]

3.2.3.1 Methods

Recruiting for this study, screening for eligibility, and the testing protocol were similar to that in phase 1.

3.2.3.1.1 Gaze tracker

For the video presentations, the non-face targets were presented in the middle of the screen twice before each pair of the target presentation (figure 3-12).

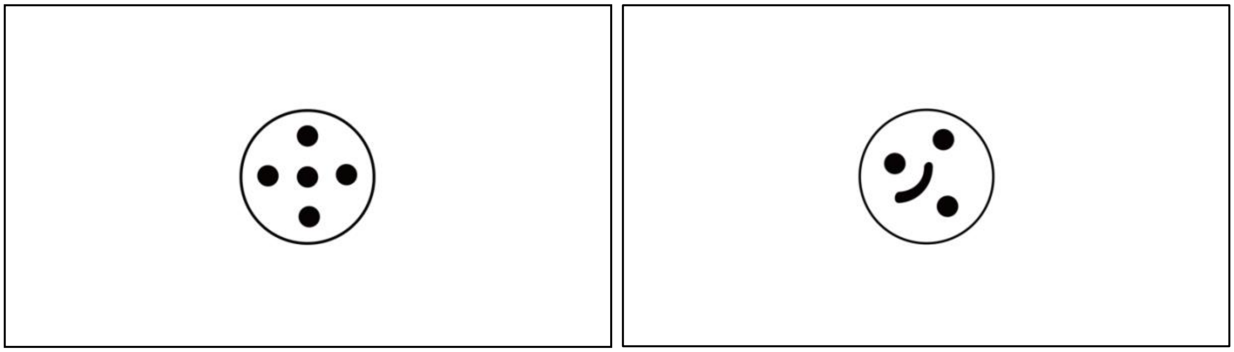


Figure 3-12. Habituation slides for the dotted-target and scrambled face as shown in the gaze tracker videos.

3.2.3.1.2 Preferential looking cards

An additional habituation card was constructed with two of the non-face target and was presented twice before each target card presentation (figure 3-13).

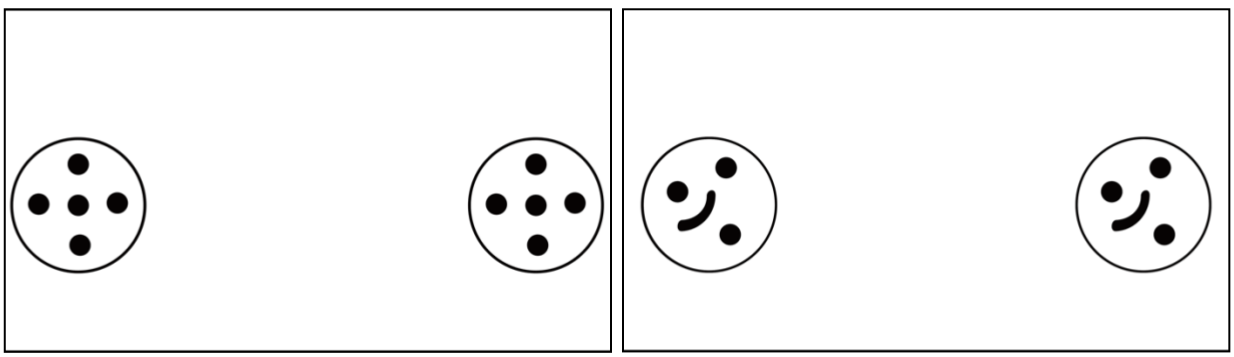


Figure 3-13. Habituation cards for the dotted-target and scrambled face.

3.2.3.2 Results

Eleven infants participated in the experiment with habituation, median age 11.5 months (range 3.5 – 15 months). Using habituation, the percentages of correct looks at the face were 45 and 55% respectively in the gaze tracker and 60 and 54% respectively for the cards.

3.2.4 Discussion and conclusion

Preference for looking at the faces was not significantly higher than looking at the comparison target either with or without habituation, and presentation in the gaze tracker did not give better results than with the cards. We suspect that the reason is that the age group is very young and thus has a very short attention span to go through recognition acuity testing. The length of the test and the difficulty of the task might be the reason for the low preference rate. The recognition task requires the participant to look at both targets and then decide, unlike the resolution task where the babies' natural eye movement as a response to the presence or absence of a stimulus is utilized. Additionally, the non-face target may be quite interesting to young babies.

In the literature, habituation was successful when done in a short experiment (20 sec).[94] In a paper by R. Fantz's,[93] the preference to look at the target stimulus was significantly higher than 50% in the first 5 trials only. We were testing their preference for faces over a series of 10 presentations, which is the minimum number needed to reach a threshold for acuity testing.[91] In addition, both papers were only studying one target stimulus. Unlike the recognition acuity testing, where threshold testing requires multiple trials that usually take longer than the babies' attention span. However, it was noted that the preference for faces was slightly stronger when presented with the dotted target rather than the scrambled face and it was chosen to be used in the following experiment.

Although the natural preference for faces (or the preference following habituation) was not sufficient in this age group, there is still the possibility that face identification can be used in a slightly older group who can be instructed to look or point to faces. This was the focus of the next study.

Chapter 4- Validation of Two Alternative Forced Choice Acuity Targets in Adults

4.1 Introduction

We designed two recognition visual acuity tests for use in infants in a two alternative forced choice card format. Each test used a different set of cards with two different optotypes; schematic Faces and Patti Pics. When developing a test of recognition acuity, it is important to compare it to the current gold standard. We validated the infant recognition visual acuity tests against the gold standard ETDRS letter chart in a group of adult participants. Validation must be done in adults because infants cannot be tested with the gold standard ETDRS.

4.2 Card design

The Face Cards were designed as per preliminary studies (Chapter 3) using Adobe Illustrator CC 2017. The Face Cards had a smiley face and a dotted target as optotypes. The Patti Pics Cards were designed with the house and circle optotypes (obtained from Precision Vision in vector files and used with their permission, Figure 4-1. The house and circle were chosen based on the similarity in design as studied by Candy et al.,[95] where confusion matrices were calculated for each optotype based on data from adult participants. The square and circle were found to be the most similar, but since they are both simple shapes they might be equally interesting to infants. Therefore, we chose the second most similar pair of optotypes which was the house and circle, with the thought that the house might be more interesting as a target because it represents an object. The card dimensions were the same as the Teller Acuity Cards (25 cm x 56 cm). The card with the largest optotypes used optotypes of 30M size (M unit = 1.5 mm).[96] The two optotypes in each card were positioned equidistant from the middle of the card and separated by 26 cm. The remaining cards were designed using the same format and followed a logarithmic scale for sizes and spacing between the optotypes. For the optotypes sizes this followed a logarithmic progression of sizes as follows: (12M, 9.5M, 7.5M, 6M, 4.8M, 3.8M, 3M, 2.4M, 1.8M, 1.5M, 1.2M, 0.95M, 0.75M, 0.6M, 0.5M, 0.4M). This is the logarithmic scale often used for logMAR charts, where the difference between each subsequent acuity level is 0.1 log unit (1.2589x).[11] Four cards were made at each acuity level, two had the target stimulus (i.e. face or house) on the right and two had the target stimulus on the left. A total of 136 cards were printed and taped onto foam boards of the same size. The cards were printed with a resolution of 2400 dots per inch.

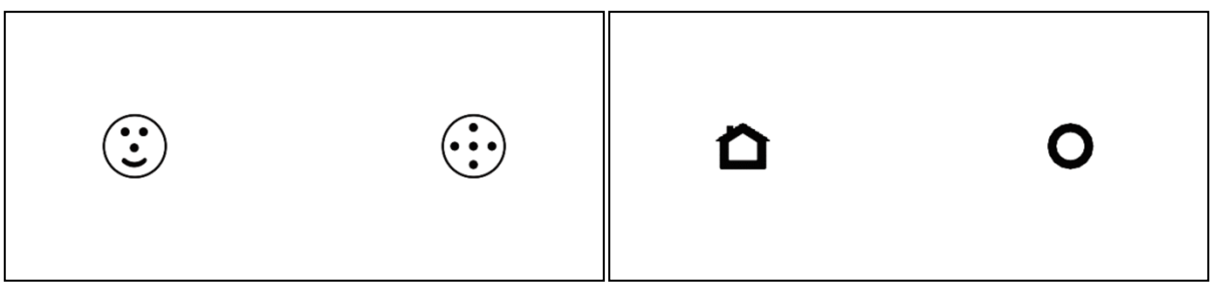


Figure 4-1. Face cards and Patti Pics Cards.

4.3 Participants

Participants for this study were recruited through invitations by email to the graduate and third year optometry students at the School of Optometry and Vision Science at the University of Waterloo. The inclusion criteria were: healthy adults, between the ages of 18 and 35 years, without any ocular conditions except for refractive error as reported by the participant. Uncorrected astigmatism was required to be below 0.75D at any meridian. The aided monocular VA required was 0.0 logMAR or better. This study was reviewed and received ethics approval through a University of Waterloo Research Ethics Committee. Informed consent was obtained from the participant prior to the testing.

4.4 Testing protocol

Each participant made one visit to the School of Optometry and Vision Science. The following tests were done to determine the participant's eligibility. Visual acuity was measured using the crowded near ETDRS chart (Precision Vision. La Salle, IL. USA) at 60 cm to the nearest line. Passing a line was when 4 or more letters on the line were correct. Distant static retinoscopy over the participant's habitual correction using lens bars, and subjective over-refraction using trial frame and lenses was performed on each eye monocularly. If both eyes met the criteria of VA and refraction, the eye with better VA and least uncorrected refractive error was chosen for the study. The participant wore their full refractive corrective (glasses or contact lenses), and recognition VA was measured using the Patti Pics Cards, Face Cards, and ETDRS in a counter-balanced order between participants, where every possible order (using permutations) of the three tests was used among the participants and assigned beforehand to each participant. The participant's task was to point at the face in the Face Cards, point at the house in the Patti Pics Cards, and name the letters on the ETDRS chart. The testing distance was 60 cm for all tests. Visual acuity was measured once for each test under three different levels of optical blur in this order, + 4.0 DS, +2.50 DS (producing 2.33DS and 0.83 DS blur at 60 cm respectively), and no blur using blurring glasses or clip-on over the participant's glasses if they were wearing any. The testing was done from highest to lowest blur so that participants would view the tests from most difficult to the least difficult, and not repeat lines close to the threshold. The examiner was blind to the position of the target stimulus for the Patti Pics and Face Cards. This was accomplished by having four cards at each level facing down so that the examiner could shuffle them and choose one to present, without seeing the stimuli. There were five presentations for each size presented in a decreasing method of limits method and skipping one size level until the participant started to make errors. Once errors were made, testing was done at every level to find the exact threshold. At least four out of five correct responses were required to pass each level. When starting the next fogging level, the testing continued at the threshold level of the previous fogging level. VA was recorded in logMAR format.

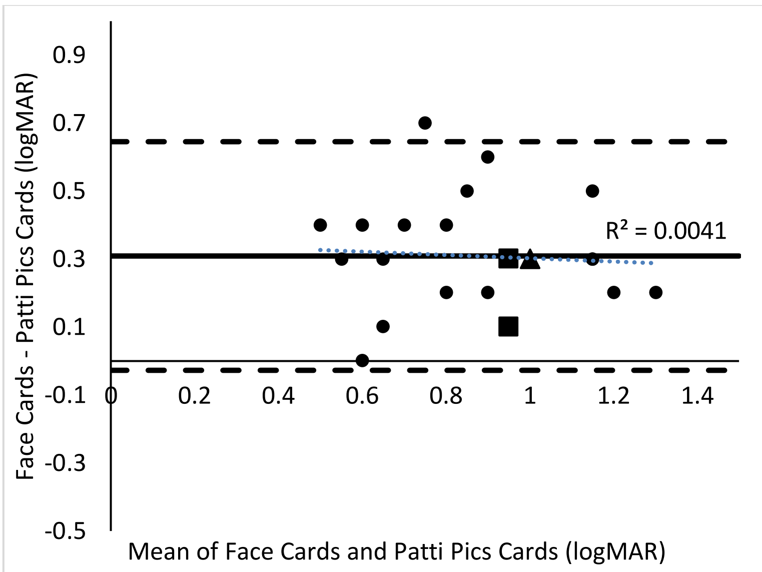
4.5 Data analysis

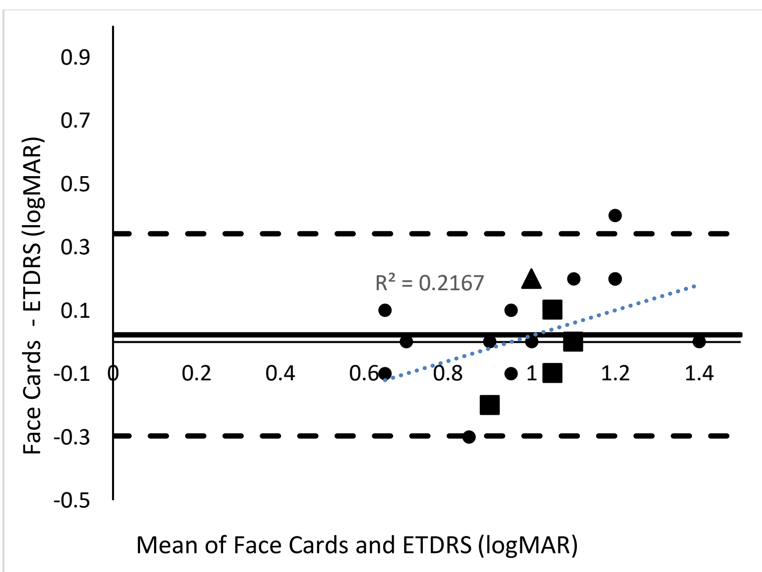
Repeated measures analysis of variance (ANOVA) was performed on the VA to determine if there was any significant difference between the Face Cards, Patti Pics Cards, and ETDRS for each fogging level using Statistica software (TIBCO Software Inc). Repeated measures ANOVA was also done to analyze the difference between any two tests across all fogging levels. Agreement between each pair of tests was calculated and displayed in Bland Altman plots[97] using Microsoft Excel software.

4.6 Results

Twenty-two participants took part in this experiment, median age 27 years (range 22 – 35). Fifteen were female and 7 were male. No uncorrected refractive error was found in any participant when over-refraction was performed.

Repeated measures ANOVA (3 x visual acuity method) for the +4D blurring lenses showed a significant effect of VA test (Face Cards, Patti Pics Cards, and ETDRS, $p < 0.00001$). Tukey HSD post hoc testing showed a significant difference between Face Cards and Patti Pics Cards ($p=0.0001$). Patti Pics Cards gave better VA values than the Face Cards by approximately three lines (0.31 logMAR). The Bland-Altman plot is shown in Figure 4-2 A. The correlation coefficient of the trend line was not significant ($r = 0.06$, $p = 0.78$), indicating no dependence of the difference on the mean VA. No significant overall or average difference was found between Face Cards and ETDRS (mean difference 0.02 logMAR, Figure 4-2 B). However, the trend line indicates that the difference significantly increased as the VA worsened ($r = 0.46$, $p = 0.03$). A significant difference was found between Patti Pics Cards and ETDRS ($p=0.0001$). The Patti Pics Cards gave better VA of about 3.5 lines (0.36 logMAR, Figure 4-2 C). The difference between the tests tended to increase as VA improved. This change was significant (r = 0.43, p = 0.04).





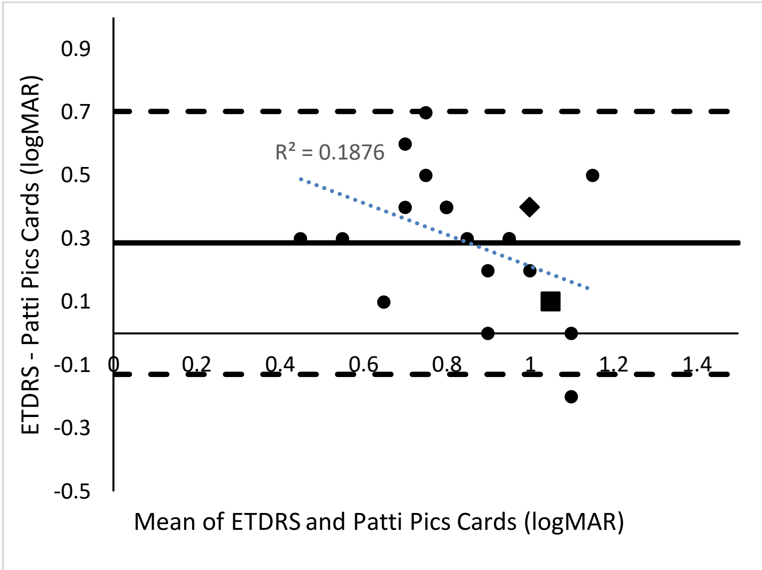


Figure 4-2. Bland-Altman plot of the difference of **A)** Face Cards and Patti Pics Cards, **B)** Face Cards and ETDRS, **C)** ETDRS and Patti Pics Cards plotted against the mean. **Viewing with** +4 D fogging lenses. The solid lines represent the mean difference, and the dashed lines are the 95% limits of agreement. The dotted lines show the trend lines.

● = one participant.

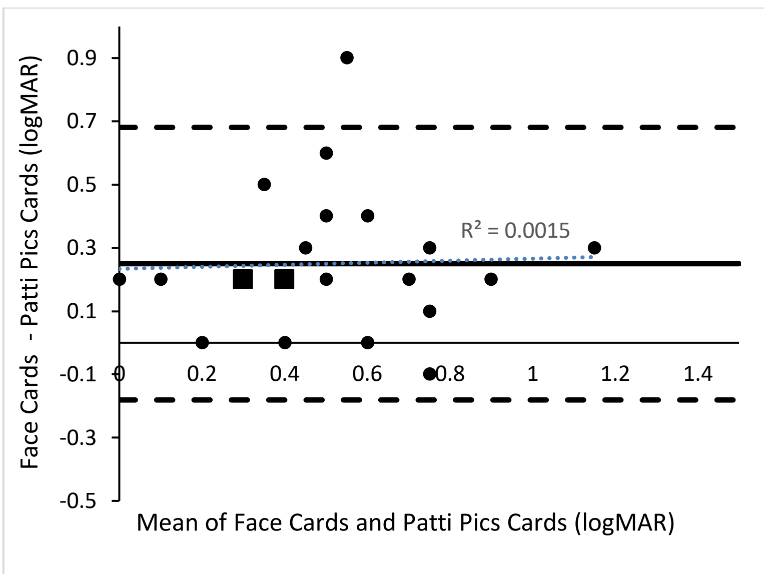
■ = two overlapping participants.

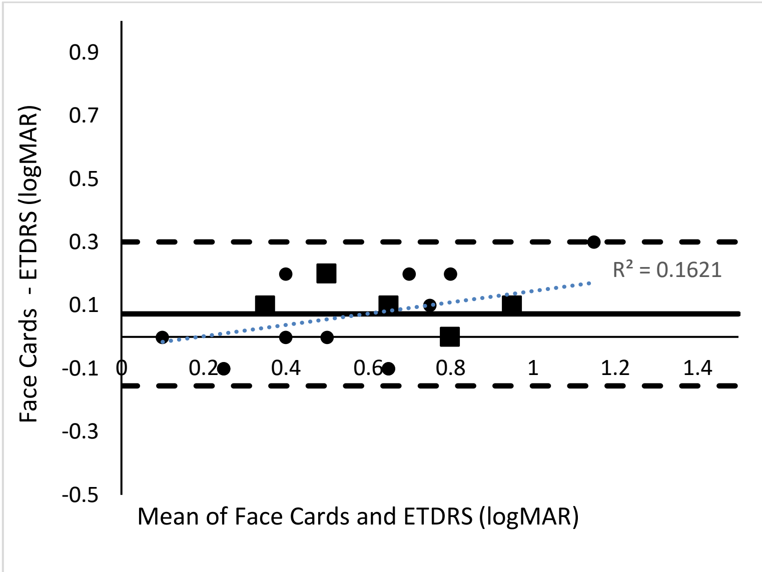
▲= three overlapping participants.

♦ = four overlapping participants.

Repeated measures ANOVA (3 x visual acuity method) for the +2.5D blurring lenses showed a significant effect of VA test (Face Cards, Patti Pics Cards, and ETDRS, $p < 0.00001$). Tukey HSD post hoc testing showed a significant difference between Face Cards and Patti Pics Cards ($p=0.0001$). Patti Pics Cards gave better VA values than the Face Cards by two and a half lines (0.25 logMAR). The Bland-Altman plot is shown in Figure 4-3 A. The correlation coefficient of the trend line was not significant ($r = 0.04$, $p = 0.86$), indicating no dependence on the mean VA. No significant difference was found between Face Cards and ETDRS (mean difference 0.07

logMAR, Figure 4-3 B). The trend line suggests that the difference increased as the mean VA worsened but this change was not significant (r = 0.4, p = 0.06). A significant difference was found between Patti Pics Cards and ETDRS (p=0.0006). The Patti Pics Cards gave better VA of about two lines (0.18 logMAR, Figure 4-3 C). The correlation coefficient of the trend line was not significant (r = 0.17, p = 0.43).





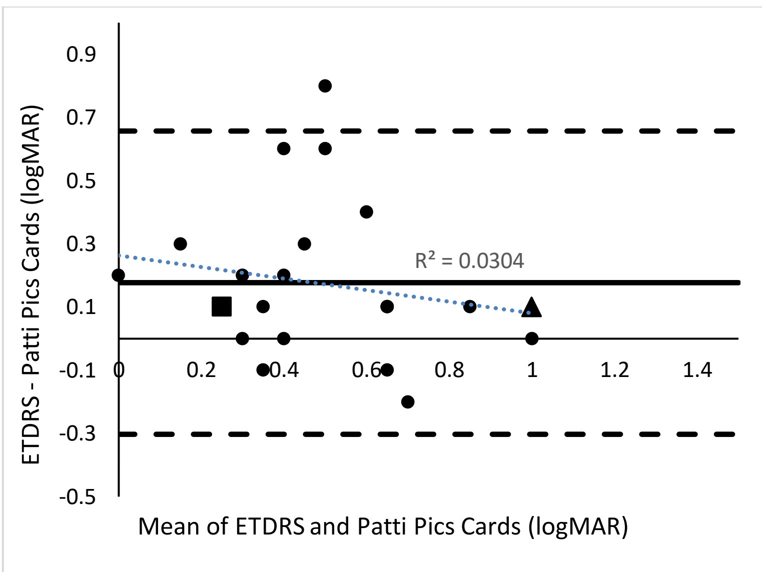


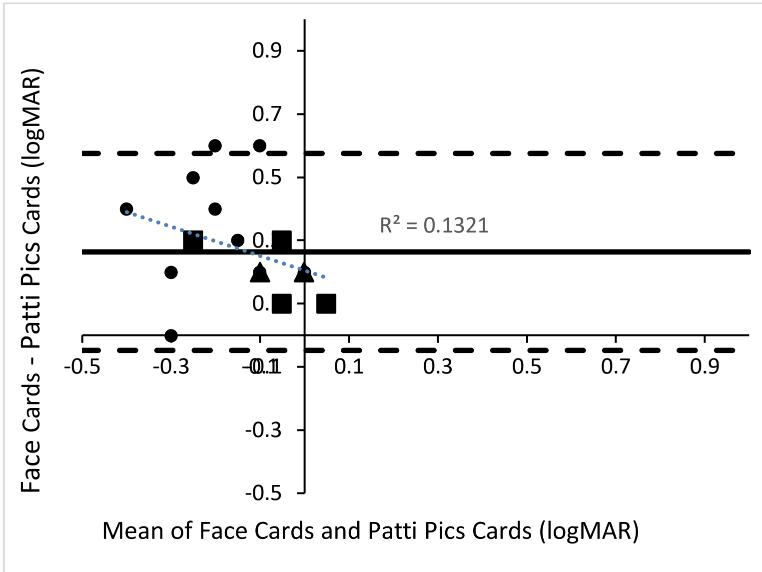
Figure 4-3. Bland-Altman plot of the difference of **A)** Face Cards and Patti Pics Cards, **B)** Face Cards and ETDRS, **C)** ETDRS and Patti Pics Cards plotted against the mean. **Viewing with** +2.50 D fogging lenses. The solid lines represent the mean difference, and the dashed lines are the 95% limits of agreement. The dotted lines show the trend lines.

● = one participant.

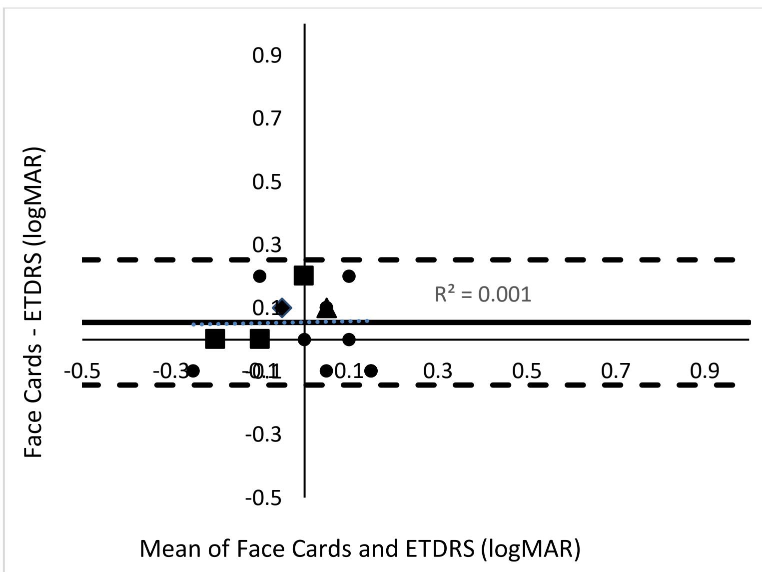
■ = two overlapping participants.

▲ = three overlapping participants.

Repeated measures ANOVA (3 x visual acuity method) for the VA without blur showed a significant effect of VA test (Face Cards, Patti Pics Cards, and ETDRS, $p < 0.00001$). Tukey HSD post hoc testing showed a significant difference between Face Cards and Patti Pics Cards ($p=0.0001$). Patti Pics Cards gave better VA values than the Face Cards by about two and a half lines (0.26 logMAR). The Bland-Altman plot is shown in Figure 4-4 A. The correlation coefficient of the trend line was not significant ($r = 0.36$, $p = 0.09$). No significant difference was found between Face Cards and ETDRS (mean difference 0.05 logMAR, Figure 4-4 B). The correlation coefficient of the trend line was not significant ($r = 0.03$, $p = 0.88$), indicating that there was no dependence on the mean VA. A significant difference was found between Patti Pics Cards and ETDRS ($p=0.0001$). The Patti Pics Cards gave better VA of about two lines (0.21 logMAR, Figure 4-4 C). The difference between the tests tended to increase as VA improved but this change was not significant ($r = 0.41$, $p = 0.06$). A summary of these results is shown in Table 4-1.



0.9
0.7
0.5
0.
0.
R² = 0.1321
-0.5
-0.3
-0.1
0.1
0.3
0.5
0.7
0.9
-0.3
-0.5
Face Cards - Patti Pics Cards (logMAR)
Mean of Face Cards and Patti Pics Cards (logMAR)



0.9
0.7
0.5
0.3
0.1
R² = 0.001
-0.5
-0.3
-0.1
0.1
0.3
0.5
0.7
0.9
-0.3
-0.5
Face Cards - ETDRS (logMAR)
Mean of Face Cards and ETDRS (logMAR)

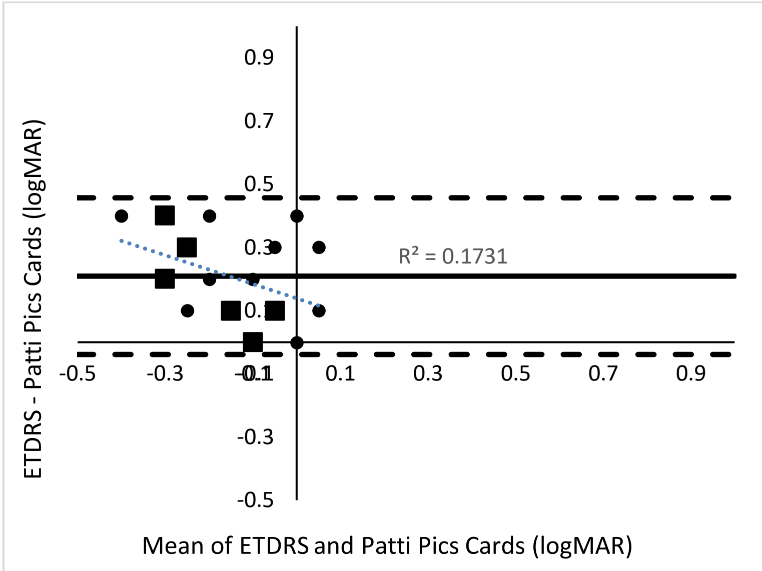


Figure 4-4. Bland-Altman plot of the difference of **A)** Face Cards and Patti Pics Cards, **B)** Face Cards and ETDRS, **C)** ETDRS and Patti Pics Cards plotted against the mean. Viewing with no fogging lenses. The solid lines represent the mean difference, and the dashed lines are the 95% limits of agreement. The dotted lines show the trend lines.
●= one participant.

■= two overlapping participants.
▲ = three overlapping participants.

Repeated measures ANOVA showed that the difference in logMAR VA between Face Cards and Patti Pics Cards was not significantly different across all fogging levels ($p = 0.5$). Similarly, the difference in logMAR VA between Face Cards and ETDRS ($p = 0.34$), and the difference in logMAR VA between ETDRS and Patti Pics ($p = 0.17$) were not significant across fogging levels.

Table 4-1. Summary of the significance between tests, mean differences, limits of agreement, and the correlation between the differences and means of each test across all fogging levels in logMAR units.

F = Face Cards, P = Patti Pics Cards, E = ETDRS, LoA = limits of agreement, UL = upper limit of agreement, LL = lower limit of agreement, r = correlation coefficient between the differences of the tests and the mean of the tests (based on the trend line shown in the plots).

Test	**+4 D**					
	ANOVA	**Mean Difference logMAR**	**LoA logMAR**	**UL logMAR**	**LL logMAR**	**r (p value)**
F - P	p =0.0001	0.31	0.33	0.64	-0.03	0.06 (p=0.78)
F - E	p=0.83	0.02	0.31	0.34	-0.3	0.46 (p=0.03)
E - P	p =0.0001	0.36	0.41	0.7	-0.13	0.43 (p=0.04)
Test	**+2.50 D**					
	ANOVA	**Mean Difference logMAR**	**LoA logMAR**	**UL logMAR**	**LL logMAR**	**r (p value)**
F - P	p =0.0001	0.25	0.43	0.68	-0.2	0.04 (p=0.86)
F - E	p=0.22	0.07	0.23	0.3	-0.15	0.4 (p=0.06)
E - P	p =0.0006	0.18	0.50	0.66	-0.3	0.17 (p=0.44)
Test	**No fogging**					
	ANOVA	**Mean Difference logMAR**	**LoA logMAR**	**UL logMAR**	**LL logMAR**	**r (p value)**
F - P	p =0.0001	0.26	0.31	0.57	-0.05	0.36 (p=0.1)
F - E	p=0.15	0.05	0.20	0.25	-0.14	0.03 (p=0.9)
E - P	p =0.0001	0.21	0.25	0.46	-0.04	0.41 (p=0.054)

4.7 Discussion

The purpose of this study was to investigate which pediatric test gives more similar VA measurements to the adult gold standard ETDRS. The results suggest that the Face Cards give a consistently closer estimate of VA than the Patti Pics Cards when compared to the ETDRS. The Face Cards gave a mean VA that was within one line of the ETDRS chart at all levels of fog, which is not considered clinically nor statistically significant.[98] On the other hand, the Patti Pics Cards gave significantly higher (better) VA results than the ETDRS at all fogging levels. These differences between Patti Pics Cards and ETDRS among the fogging levels seemed more variable than those between the Face Cards and the ETDRS and also more variable than between the Face Cards and Patti Pics Cards. The differences were 0.36, 0.18, 0.21 logMAR; 0.02, 0.07, 0.05 logMAR; and 0.31 0.25 0.26 logMAR respectively. However, it is important to note that the differences between tests were consistent across fogging levels for all tests i.e.there was no effect of fogging level on the differences between the tests.

We compared the Face Cards and the Patti Pics Cards to the ETDRS chart because ETDRS was designed to optimize the measurement of VA in adults and has become one of the gold standards for VA measurement.[13,99] We attribute the differences of VA found in this study to the following differences in the test design. First, we tested these charts in the same format as they would be used clinically and the number of optotypes in each test was not the same, possibly affecting the VA outcome. In the gold standard ETDRS, there are 10 Sloan letters used in the chart, meaning that the likelihood of getting the correct answer by guessing is 1 out of 10 or 0.1. However, the patients (or participants) are not usually aware of this, and they base their answers on all the letters of the English alphabet, in which case the guessing rate is 1 out of 26 or 0.038. Alternatively, in the 2AFC the guessing rate is 1 out of 2 or 0.5, which is much higher than for the ETDRS. This means that, when presenting the cards closer to the threshold level, the participants are more likely to get the correct answer by chance for the Face Cards and Patti Pics Cards than in the ETDRS. We required at least 4 out of 5 correct responses to pass each level in all tests in an attempt to accommodate for this difference. However, the overall guessing rate is still lower in the ETDRS. This may explain some of the difference between the Patti Pics and ETDRS.

Second, the optotype design and overall size could affect the VA. The face/ non-face optotypes were designed so that the width of the details are equal to the width of the stroke of the letters in the ETDRS. These details are the eye, nose, and mouth. Thus, the face and dotted target have fewer (and detached) details, rather than a continuous line such as in letters and Patti Pics symbols. In addition, the outline of the optotypes in the Face Cards are similar (round) while all the optotypes in the ETDRS and Patti Pics have different outlines. This may make the faces/dotted-targets more difficult to identify. Mercer et al.[100] compared VA from Patti Pics and ETDRS presented in one line and surrounded by a crowding box. The mean difference between the tests was only 0.01 logMAR. Bailey et al.[31] also showed a one letter difference (0.02 logMAR) between the Patti Pics and ETDRS when presented in a distant crowded chart. Because both the Patti Pics and the ETDRS had identical presentation styles in both these studies, this indicates that the difference in the current study may be due to optotype formatting and the amount of crowding. The Patti Pics are available in a crowded format with crowding bars around them, but in the current study, we chose those without crowding bars to simplify the task as much as possible for the infant participants. These findings suggest that the Patti Pics and ETDRS have a very similar optotype design.

Third, the presence or absence of crowding may influence the VA measurement. As discussed in chapter 1, the full ETDRS chart has five letters per line and equivalent spacing between the lines and letters. This gives equal crowding among all acuity sizes. In the Face cards, the outline of the face/dotted-target was implemented using a specific width of the edge of the face, which was chosen to give equal acuity to the ETDRS chart and which we think gives an equivalent crowding phenomenon to the Sloan letters in an ETDRS format. Additionally, the face/dotted-target have separate elements within the optotype as mentioned previously. On the other hand, the crowded phenomenon is absent in the Patti Pics Cards.

Since the Patti Pics gave better VA than the ETDRS when presented in 2AFC and a similar VA when presented in a similar format as the ETDRS, we can conclude that these differences are due to the 2AFC (2AFC methods yield higher VA than the full chart) and the lack of crowding. The use of more complex optotypes (face/dotted-target) which include aspects of crowding gave a similar VA to the gold standard (compensating for the difference in presentation) and resulting in an overall similar measurement of VA.

Chapter 5- Infant Feasibility Study

5.1 Introduction

In order to develop a test of recognition acuity in this infant age group, many factors should be considered. An important aspect when designing a test is the level of difficulty of the test. Infants' cognitive abilities should be at the same level or above that required by the test to give reliable responses. Secondly, it must be interesting and engaging for the targeted age group in order for them to be willing to do the test. The preferential looking technique was not successful in the babies (Chapter 3), but pointing or looking responses may be successful in the 2AFC paradigm when tested in slightly older infants who can respond to instructions.

In this study we tested two recognition visual acuity tests using two alternative forced choice cards, validated in adults in the previous experiment (Chapter 4). We tested the feasibility of using the 2AFC method to measure recognition VA in infants between the ages of 16 – 42 months, in terms of the testability and ability to measure a VA threshold. Additionally, the development of recognition VA across this age group was observed.

5.2 Participants

Participants were recruited for this study through; the clinic lists of patients who had given permission to be contacted about research opportunities, distributing flyers to the daycare facilities in the Kitchener/Waterloo area, and by sending emails to graduate students, staff and faculty in the School of Optometry. Inclusion criteria were similar to that in the preliminary study and were as follows: 1) no significant ocular health conditions (e.g. strabismus); 2) gestational age more than 37 weeks at birth, normal development/ meeting developmental milestones, and no significant general health problems as reported by parents; 3) refractive error that does not exceed 2.5D hyperopia, 1D myopia or 1D astigmatism at any meridian or anisometropia >1D in any meridian when measured with non-cycloplegic static retinoscopy;[63] 4) binocular resolution visual acuity measured by Cardiff cards at 1 meter equal to or above normal limits[43], see Table 5-1. The study was reviewed and received ethics approval through a University of Waterloo Research Ethics Committee. Informed consent was obtained from the parent or guardian prior to the testing.

Table 5-1. Resolution VA inclusion criteria according to age, as measured by Cardiff Acuity Cards at 1 meter.[43]

Age (months)	**Binocular VA**	
	Snellen meter	logMAR
12 - 17	6/12 – 6/50	0.3 – 0.9
18 - 23	6/8 – 6/27	0.12 – 0.6
24 - 29	6/6 – 6/18	0.0 – 0.5
30 - 36	6/5.5	-0.08

5.3 Screening for eligibility

For all the testing, the participant was seated on their parent's/guardian's lap. The following tests were performed to determine the infant's eligibility. All tests were done under binocular viewing.

Ocular alignment was assessed by Hirschberg test and cover test. For the cover test, the thumb was used as an occluder and a finger puppet as a target. Ocular motility was assessed using a finger puppet. Distant static retinoscopy was performed with lens bars, +2D pediatric blurring glasses and a TV with a cartoon playing as a distant viewing target to relax the infant's accommodation, and VA with Cardiff Cards. In order to maintain the child's interest and cooperation, the retinoscopy and VA with Cardiff cards were spread through the first or second visit instead of prior to testing as usually done in research studies. The reasoning was that VA measurement is one of the first measures performed in a clinical setting, and so we wanted the child to be fresh for the VA measures that were outcome measures. Additionally, retinoscopy does not involve the child's responses in the same way as a VA test, and therefore varies the task for the child, in order to maintain their cooperation.

5.4 Visual acuity testing protocol

The Face Cards and the Patti Pics Cards were tested in a counter-balanced order, meaning that every possible order (using permutations) of the tests was used and assigned beforehand to each subject. The Face Cards and the Patti Pics Cards were tested on two different visits to avoid fatigue or boredom by the infant. The visits were planned to be one week apart. This was because infants of this age develop quickly and they may learn new skills and thus perform better on the second visit as a result of general development. If the infant was not testable on the first set of cards, the study would continue and both acuity cards would be tested in the same visit. The visual acuity was tested binocularly and at a 60cm testing distance. This testing distance was chosen to be at a point as far as possible which would allow the child to point. Using a closer distance than this would have required the smallest optotypes to be too small for the resolution limit possible with printing. Two 30M size cards of the selected acuity cards (Face Cards or Patti Pics Cards) were introduced as training cards with the target stimulus once on each side. The participant was shown the target stimulus and asked to point or look at the target stimulus with the help of the examiner. Testability was measured next, whether the participant passed the training or not, using all of the four 30M cards. At this step, the examiner was blind to the position of the target stimulus. Three out of four correct responses were required for the participant to be considered testable.

If the participant was testable, visual acuity measurement followed starting at four lines larger than the binocular lower 95% VA for the child's age based on the norms for the Cardiff Acuity Cards (Table 5-2). The measurement was done using a two down one up staircase method. The step size was two acuity levels until close to the threshold level and step size became one acuity level when the participant started to make errors. The VA threshold was defined as the smallest optotypes for which at least four out of five responses were correct. VA was recorded in logMAR format.

Testability of matching Patti Pics was performed for comparison using the commercially available uncrowded matching Patti Pics flip-book format (Precision Vision. La Salle, IL. USA), at two distances 60 cm and 3m. It was done at 60 cm to be similar to the 2AFC tests, and 3 m as it is typically done in clinical testing. A key card was held by the parent and the infant was instructed to point at the optotype on it. There was no formal training phase for this test, but the infant was introduced to the test, as typical in a clinical setting. The examiner presented four different targets of the 30M size at the testing distance. At least 3 out of 4 correct responses were needed to be considered testable Resolution acuity was measured by Cardiff acuity cards at 1 meter for comparison and for eligibility in the standard clinical way.

Table 5-2. Starting level for recognition VA testing based on the resolution VA age norms for Cardiff Acuity Cards.

Age Groups	**lower 95% resolution VA**	**Starting level**	
		Snellen meter	**logMAR**
15 – 19	6/50	6/120	1.3
20 – 23	6/30	6/76	1.1
24 – 27	6/18	6/50	0.9
28 – 31	6/18	6/50	0.9
32 – 36	6/12	6/30	0.7

5.5 Data analysis

Testability percentages and ratios of the number of testable participants to the total number of participants were calculated for the Face Cards, Patti Pics Cards, and matching Patti Pics. Repeated measures analysis of variance (ANOVA) using Statistica (TIBCO Software Inc) was performed on VA measurements to compare VA with Face Cards, Patti Pics Cards, and Cardiff Acuity Cards. Agreement for VA between each pair of tests was calculated and displayed in Bland Altman plots[97] using Microsoft Excel software. Correlation between the VA with each test and age was calculated, and the resulting slopes were compared using Systat (Systat Software, Inc).

5.6 Results

5.6.1 Testability

Seventeen infants took part in this study, median age 27 months (range 16 – 42 months). Overall testability of Face Cards was 70.5%, while the testability of the Patti Pics Cards and matching were both 64.7%. Testability in infants 26 months or older was 100% for all tests. Table 5-3 shows testability for all participants. Three infants passed the training for the Face Cards but not the testability. Another participant passed the testability for the Face Cards but we were unable to get a VA threshold, due to lack of cooperation. Five participants (four of whom are mentioned previously) passed the training for the Patti Pics but not the testability. It was observed that that training and testability phase was quicker with the Face and Patti Pics Cards than with the Patti Pics matching test.

Table 5-3. Testability, training, and visual acuity results for all participants sorted by age from young to old. Red area denotes infants who were not testable.

Age (months)	**Face Cards**			**Patti Pics Cards**			**Passed testability with matching Patti Pics**	**Cardiff Cards VA (logMAR)**
	Passed training	**Testability (number correct)**	**VA (logMAR)**	**Passed training**	**Testability (number correct)**	**VA (logMAR)**		
16	Yes	3/3	NA	Yes	1/4	NA	No	0.3
18	Yes	1/3	NA	Yes	0/2	NA	No	0.7
18	Yes	3/3	1.3	Yes	3/3	1.2	Yes (by naming)	0.2
19	Yes	2/4	NA	Yes	0/3	NA	No	0.3
20	No	2/6	NA	Yes	1/3	NA	No	0.7
21	Yes	2/4	NA	Yes	1/4	NA	No	0.6
25	No	1/3	NA	No	1/3	NA	No	0
26	Yes	3/3	0.4	Yes	3/3	0.1	Yes	0.2
27	Yes	3/3	0.3	Yes	3/3	0.3	Yes	0
27	Yes	4/4	0.5	Yes	3/3	0.3	Yes	0.2
30	Yes	3/3	0.4	Yes	3/3	0.3	Yes	0
34	Yes	3/3	0.4	Yes	3/3	0.3	Yes	0
36	Yes	3/3	0.5	Yes	3/3	0.1	Yes	0
36	Yes	3/3	0	Yes	3/3	0.1	Yes	0.2
36	Yes	3/3	0.3	Yes	3/3	0.1	Yes	0
37	Yes	3/3	0.4	Yes	3/3	0.1	Yes	0
42	Yes	3/3	0.1	Yes	3/3	0	Yes	-0.1
Total	**15/17 (88%)**	**12/17 (70.5%)**	**Mean = 0.42 Mean without outlier = 0.33**	**16/17 (94%)**	**11/17 (64.7%)**	**Mean = 0.26 Mean without outlier = 0.17**	**11/17 (64.7%)**	**Mean = 0.19**

5.6.2 Comparison of VA between tests

For those infants for whom a measure of VA was obtained, repeated measures ANOVA (3 x VA tests) showed a significant difference between all tests ($p < 0.00001$). Table 5-4 shows the mean differences and 95% limits of agreement between the tests. Tukey HSD post hoc showed no significant difference between Face Cards and 2AFC Patti Pics Cards (mean difference = 0.15 logMAR). The outlier shown in Figure 5-1 did not have a major effect on the mean difference between the Face Cards and Patti Pics Cards (mean difference without the outlier was 0.16 logMAR). However, the post hoc test showed a significant difference in this case. The trend line in Figure 5-1 indicates that there is no significant correlation between the mean and the difference between the tests ($r = 0.05$, $p = 0.9$). A significant difference ($p=0.0007$) was found between Face Cards and Cardiff Acuity Cards (mean difference = 0.35 logMAR), where the Face Cards gave poorer VA. The mean difference was reduced to 0.28 logMAR when the outlier was removed, which was still a significant difference. A significant correlation coefficient ($r = 0.86$, $p = 0.0002$) indicates that the difference between the tests increased as VA worsened (Figure 5-2), although when removing the outlier, the correlation was no longer significant. A significant difference ($p=0.049$) was found between the 2AFC Patti Pics Cards and Cardiff Acuity Cards (mean difference = 0.2 logMAR). The mean difference was reduced to 0.12 logMAR when the outlier was removed, which is not a significant difference. Figure 5-3 shows a significant correlation coefficient ($r = 0.76$, $p = 0.03$), meaning that the difference increased as VA worsened, but again by removing the outlier the correlation was no longer significant.

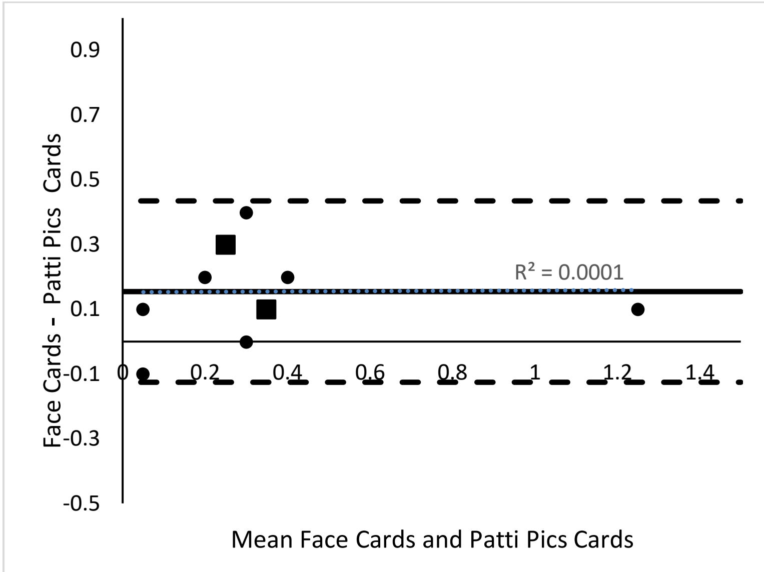


Figure 5-1. Bland-Altman plot of the difference of the Face Cards and Patti Pics Cards plotted against the mean. The solid line is the mean difference, and the dashed lines are the 95% limits of agreement. The dotted line is the trend line.

●= one participant.

■= two overlapping participants.

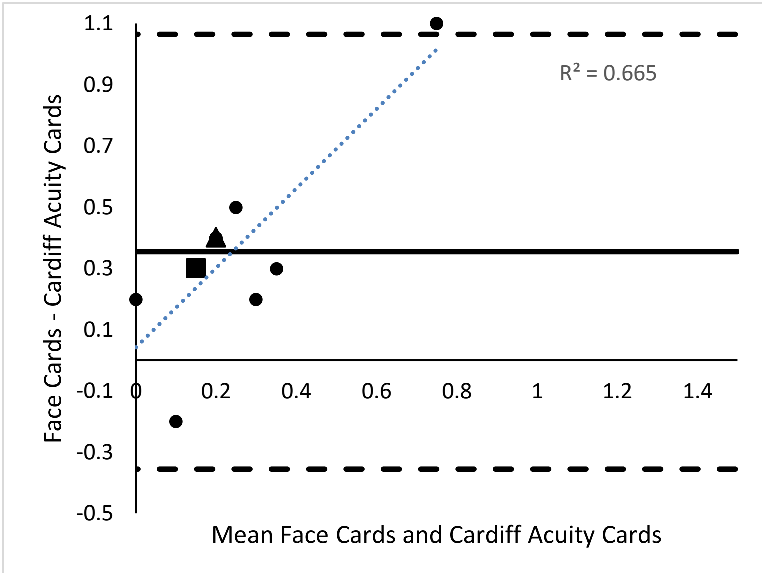


Figure 5-2. Bland-Altman plot of Face Cards and Cardiff Acuity Cards plotted against the mean. The solid line is the mean difference, and the dashed lines are the 95% limits of agreement. The dotted line is the trend line.

●= one participant.

■= two overlapping participants.

▲ = three overlapping participants.

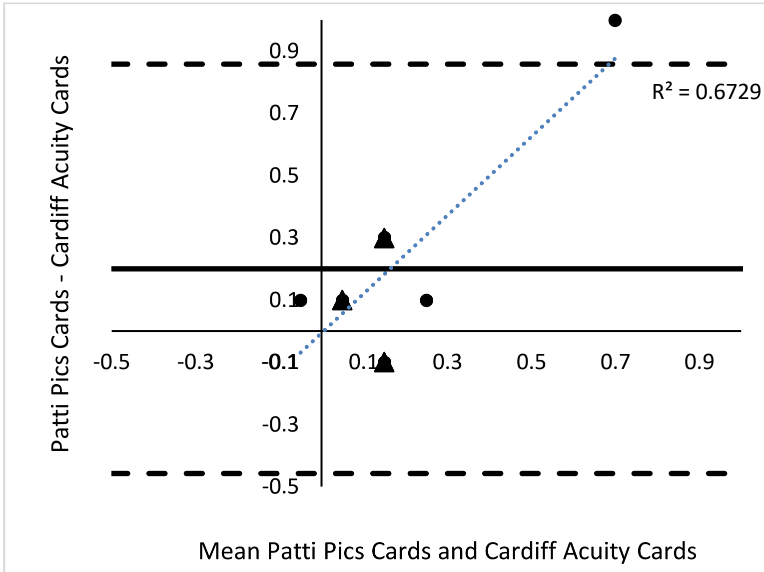


Figure 5-3. Bland-Altman plot of Patti Pics Cards and Cardiff Acuity Cards plotted against the mean. The solid line is the mean difference, and the dashed lines are the 95% limits of agreement. The dotted line is the trend line.

●= one participant.

▲= three overlapping participants.

Table 5-4. Summary of the significance between tests, mean differences, and limits of agreement. F = Face Cards, P = Patti Pics Cards, C = Cardiff Cards, LoA = limits of agreement, UL = upper limit of agreement, LL = lower limit of agreement.

Test	**ANOVA**	**Mean difference**	**LoA**	**UL**	**LL**
F - P	p=0.15	0.15	0.28	0.43	-0.12
F - C	p=0.0007	0.35	0.71	1.06	-0.36
P - C	p=0.049	0.20	0.65	0.85	-0.45

5.6.3 Correlation between age and VA

A significant correlation was found between VA and age for each test. The correlation coefficient between Face Cards and age was r = 0.76, p = 0.006. The correlation coefficient between the Face Cards and age did not reach significance with the outlier removed (r=0.49, p=0.15). The correlation coefficient between 2AFC Patti Pics Cards and age was r = 0.8, p = 0.003 and when the outlier was removed this changed to r=0.68 p=0.03. The correlation coefficient between Cardiff Acuity Cards and age was r = 0.72, p = 0.001. Figure 5-4 shows the correlation between VA and age for each test.

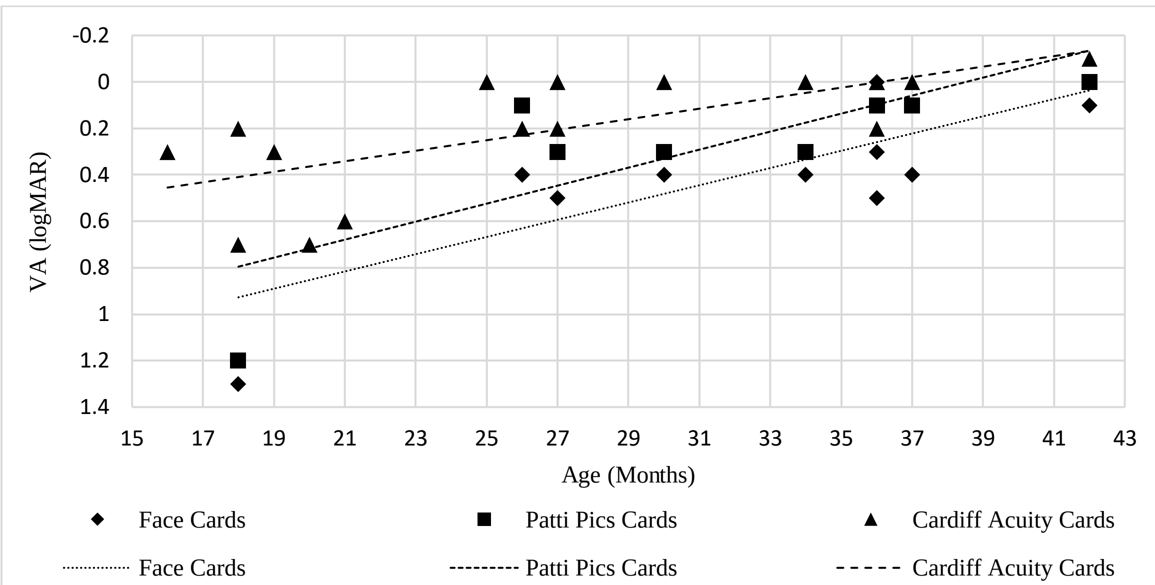


Figure 5-4. Scattergram showing the correlation between each VA test and age with regression lines for each.

No significant difference (p = 0.27) was found between the slopes of the Face Cards vs age (slope = 0.037) and the Cardiff Acuity Cards vs age (slope = 0.023). There was still no significant difference in these slopes when the outlier was removed (p = 0.46). No significant difference (p = 0.18) was found between the slopes of the 2AFC Patti Pics Cards vs age (slope = 0.039) and the Cardiff Acuity Cards vs age (slope = 0.023). Or between the slopes of the

2AFC Patti Pics Cards vs age and the Cardiff Acuity Cards vs age when the outlier was removed (p = 0.35). No significant difference was found between the slopes of Face Cards vs age and 2AFC Patti Pics Cards vs age (p = 0.94), and when the outlier was removed for both 2AFC Patti Pics Cards vs age and Face Cards vs age (p = 1). The slope analysis is summarized in Table 5-5.

Table 5-5. Summary of slope analysis

Test	**p-value**
Face Cards and Cardiff Acuity Cards	0.27
Face Cards (w/out outlier) and Cardiff Acuity Cards	0.46
Patti Pics Cards and Cardiff Acuity Cards	0.18
Patti Pics Cards (w/out outlier) and Cardiff Acuity Cards	0.35
Face Cards and Patti Pics Cards	0.94
Face Cards and Patti Pics Cards (w/out outlier)	1

5.7 Discussion

The aim of this study was to determine if pointing or looking responses could be used to measure recognition acuity at a younger age than what is currently possible by matching.

5.7.1 Training

The infants' responses during the training were different between the two card tests. One infant passed the training for the Patti Pics Cards but not the Face Cards. On the other hand, one infant passed the testability for the Face Cards Cards but not the Patti Pics. This may just be due to different levels of cooperation on different days for these infants, and may not be significant. The fact that some infants passed the training but not the testability may indicate that they understand the task required of them but their attention was not enough to perform more presentations (testability and then VA). More infants passed the training for Patti Pics than those who passed the training for the Face Cards. Based on the observation of the infants' behavior, one reason for this might be because of the familiarity of both optotypes used in the Patti Pics Cards. The infants may be familiar with simple pictures of a house and perhaps a circle and they can respond to the task of differentiating which is the house. On the other hand, the non-face target on the Face Cards is unknown to the infants, which may cause some confusion as to what the task is asking of them. Also, the lack of familiarity of the non-face target may make it interesting to the infants.

5.7.2 Testability

The testability was almost equal among all tests (Patti Pics Cards, Face Cards, and matching Patti Pics Cards). Only one participant could do the Face Cards and not the other tests, although VA could not be obtained from that participant.

It was observed that the training and testability phase was quicker with the Face and Patti Pics cards than with the Patti Pics matching test. This was because in the case of 2AFC the infant only had to be trained to point at the target stimulus, while in the matching format the infant has to be trained, and become familiar, with all five optotypes used in the test.

Looking did not yield accurate responses for the Patti Pics Cards or Face cards. This may be because the infant is required to observe both optotypes on the card and then decide which one is the correct answer. This results in a complex looking pattern between the two optotypes, which makes it challenging to asses the response based on observation. Testability and VA were recorded by looking responses for one participant only (age 18 months). It is important to note that the measured recognition VA for this participant was very low.

In our study, the testability of using the 2AFC method was 100% in infants 26 months old and older. On the other hand, recognition VA using the matching technique was only reliably tested in infants aged 36 months old or older.[90] Ciner et al.[86] found that when using the matching LEA symbols, recognition VA was only testable in 75% of infants aged 42 months. Similarly, Shallo-Hoffmann et al.[89] and Cyert[101] found that the testability in 48 month olds was 95% and 99% respectively. Our results seem to indicate that the 2AFC cards enabled testing of recognition acuity to a younger age. We already know that the use of the 2AFC method was successful in younger age groups (0 – 24 months) for resolution acuity in other studies.[22] Resolution VA results were obtained in 100% of infants as young as 1 month old using the Teller Acuity Cards.[36] In these cases, the task was to identify the presence or absence of a stimulus [22,23] using the infant's natural preference to look at a pattern rather than a blank space.[5] The task is similar for the Cardiff cards, as the child has to look towards a stimulus rather than no stimulus. In our study, the task was more difficult. It was based on the infants' ability to recognize and differentiate between two optotypes, one of which was the preferred target.

The Patti Pics matching task showed a testability of 70% in the 16 – 42 months in our study, a 100% testability in the 26 – 42 months subgroup, and 14% of the 15 – 25 months subgroup. The literature indicates that the testability using LEA symbols matching test of a similar age group (30 – 36) is 75%, and increases to 95% by 48 months.[86,90] Thus the matching test was successful at a younger age in the current study compared to previous studies. This might be because of the reduced number of participants at each age in the current study.

5.7.3 VA

In the current study, the Patti Pics Cards gave acuity of 1.5 lines better than the Face Cards and the values of VA according to age are given in Table 5-5. To date, currently available data on recognition VA in infants is very limited, starts from the age of 33 months and is undertaken with matching tests. The available data and test used vary in the current literature, and include letter matching[42,46] and Landolt Cs[44]. The mean VA and 95% confidence intervals from previous studies are shown in Table 5-5. Stiers et al.[44] used uncrowded Landolt Cs to measure recognition acuity in this age group and showed better VA than letter tests and both Patti Pics Cards and Face Cards in our study. Drover et al.[46] and Leone et al.[42] used HOTV letters surrounded by crowding bars. Their results were similar to the results of the Patti Pics Cards in our study (0.08, 0.09, and 0.1 logMAR in 36 months olds and 0.08, 0.05, and 0 logMAR in 42 months old for Drover et al, Leone et al, and our study respectively). On the other hand, when Leone et al. used ETDRS and HOTV in single line presentations, the results were lower (poorer) and between the Patti Pics and Face Cards VA found in our study. These findings agree with the adult study, where the Face Cards were more similar to the ETDRS.

Table 5-6. Mean (95% confidence interval) of recognition VA values according to age in logMAR.

Age	Current study		Stiers et al.[44]	Drover et al.[46]	Leone et al.[42]	
	Face Cards	Patti Pics Cards	Uncrowded Landolt C	Crowded HOTV	Crowded HOTV	line ETDRS/HOTV
26	0.4	0.1				
27	0.3	0.3				
27	0.5	0.3				
30	0.4	0.3				
34	0.4	0.3	-0.1 (-0.18 – -0.02)		0.13 (0.11 – 0.15)	0.25 (0.20 – 0.30)
36	0.5	0.1		0.08 (0.29 – -0.13)	0.09 (0.07 – 0.10)	0.22 (0.17 – 0.26)
36	0	0.1				
36	0.3	0.1				
37	0.4	0.1	-0.13 (-0.22 – -0.04)		0.07 (0.05 – 0.09)	0.16 (0.14 – 0.18)
42	0.1	0	-0.12 (-0.24 – 0)	0.08 (0.25 – -0.09)	0.05 (0.03 – 0.06)	0.15 (0.12 – 0.18)

In our study, all three tests significantly correlated with age. The Patti Pics Cards and the Face Cards showed different absolute recognition acuity levels, but they correlated to age similarly ($r = 0.8$ and 0.76 respectively). The resolution acuity measured by Cardiff Acuity Cards was similarly correlated to age ($r = 0.72$). There was no significnat differences in the slops of the regression lines with age, which indicates that all the tests mature at the same rate.

The literature shows a strong relationship between VA and age. As soon as the Teller Acuity Cards and Cardiff Acuity Cards were made, normative data using these tests were established, and showed an increase of resolution acuity with age; 1 cpd (1.5 logMAR) at 1 month of age increasing to 30 cpd (0 logMAR) at 3 years of age (see Tables 1.1 and 1.2).

When comparing recognition acuity values against age, the literature is inconclusive about when recognition acuity is adult-like. One study indicated that by 5 years of age children reached adult levels for Landolt Cs.[45] However, other studies investigated recognition acuity values using letter charts and showed adult levels around 8 – 9 years of age.[7,46] In our study, all infants aged 36 months or older had a recognition VA of 0.1 logMAR or better when measured with the Patti Pics Cards, in addition to one 26 month old participant who also reached 0.1 logMAR. Similar values were found when using Landolt C[44] and single surrounded HOTV[42]. Moreover, in the current study, only two infants reached these levels with the Face Cards (one 36 month old and one 42 month old).

Chapter 6- General Discussion and Conclusion

6.1 Discussion

Measuring recognition acuity is very important in infants. It is necessary to accurately assess and monitor their visual development, especially in cases where amblyopia is suspected. It is also important to monitor visual acuity changes during treatment for amblyopia and other conditions. In order to create and validate such a test, a series of experiments were conducted. Firstly we designed the optotypes following the established standards of visual acuity charts,[11] and tested these optotypes in adults with normal vision. Adjustments were made and the optotypes were re-tested to develop the optimum version of the optotypes.

When developing the face targets, we found that varying the width of the outline affected the VA and this might be because of crowding. This might have caused the VA with face targets used in the Face Cards to be similar to the full ETDRS chart as they are effectively a crowded stimulus, while the Patti Pics symbols were not a crowded stimulus. Crowding elements can be added to Patti Pics (crowding bar or box), but the uncrowded version was used to simplify the task as much as possible.

After the Face/ non-face combination was chosen, the next step was establishing the best presentation method for the targeted age group. The 2AFC method was chosen since it is the current method for testing infants for resolution acuity[22,23]and stereo acuity.[102] A non-contact gaze tracker and a set of cards were used to test the preference to look at the smiley faces in infants aged 3 – 20 months old. Similar results were found between the gaze tracker and the cards, but the preference to look at faces was not sufficiently strong or consistent to be used to measure visual acuity. The first 2 or 3 looks were towards the face but this was not sufficient to measure VA. Even with the use of habituation, the preference was not strong enough. To reach a VA threshold, a series of at least 12 looks is required, and these looks must be consistently towards the target if the target is visible. Previous studies with babies have successfully used habituation, but these studies measured fewer responses with each infant i.e. they did not attempt to measure a threshold on an individual infant.[94]

In the main experiment, I eliminated the gaze tracker (as this did not result in better responses) and used an older age group. We observed both the infants' looking and pointing responses since they were old enough to respond to instructions. I also included a similar set of cards made with Patti-Pics symbols. The majority of the participants above 26 months were able to point at the target stimulus, but the looking responses were inconclusive because of the nature of the recognition stimulus compared to the resolution stimulus. The looking responses were the natural behavior toward the presence of a stimulus, and the infants seemed equally likely to fixate the non-target stimulus. But pointing is a more deliberate response as a result of instruction.

6.1.1 Adults vs infants

Similar patterns were detected in both adult and infant studies, and the pattern of these differences were similar when the infant outlier was removed. The Patti Pics Cards gave better VA than the Face Cards by two and a half to three lines (a significant difference) among the fogging levels in the adult study. While in the infant study the Patti Pics Cards gave better VA of one and a half lines only. This this difference was not significant, but became significant with the outlier removed. Ideally, the differences should be equal in adults and infants. Behavioral factors may have affected these results in the infant's study. This may be because the infants performed relatively more poorly in the Patti Pics (or better in the Face Cards) because they were more interested in the Faces. Another reason for this difference may be the difference in sample size between both groups (adults N = 22, infants N = 11).

Due to the number of participants in the adult group, and the use of the ETDRS to compare the results we can conclude that the true differences between the tests are shown in the adult group. On the other hand, the infant group provided an estimate of the normal values of recognition acuity in this age group and how it relates to the resolution acuity measured by Cardiff Acuity Cards. These findings are some of the first reported levels of recognition acuity in infants of 26-30 months and show the potential of this format for VA testing in this young age group. Developing such a test may be helpful in obtaining more data of recognition VA in infants of this age, and clinically help detect any abnormalities that may cause reduction in recognition VA.

My hypotheses were as follows.

1) Recognition visual acuity is measurable using looking or pointing responses in a 2AFC format at a younger age than is measurable with matching. The testability findings in our results reject this hypothesis. However, testability with the Face and Patti Pics cards was better at younger ages than reported for matching in the literature. It was observed that it took longer to determine testability for matching than testability of 2AFC. Timing these phases would be of value. Infants' attention span is relatively short, and by using a test that takes less time, reliable measurement more likely can be obtained before the infant loses interest. This conclusion was drawn based on the testability results. Different results may be obtained if VA using matching Patti Pics had been measured, and the number of infants who could reach a threshold compared between the techniques (matching vs 2AFC).

2) Face targets have better testability than Patti Pics symbols in infants aged 16 to 42 months. The testability of Face Cards was 70.5% while the testability of the Patti Pics Cards was only 64.7%. However, the difference here is only one participant. Therefore, this hypothesis is tentatively accepted. More participants are needed to be more conclusive about this hypothesis.

3) Testability increases over the age range 16-42 months. This hypothesis was proved correct. Testability at 26 months of age upward was 100%, while the testability of infants under 26 months was 14.3% (1 out of 7). The change in testability percentage seems to be abrupt

because at 26 months the testability changes from 14.3% to 100%. There were gaps at certain ages in our sample (e.g. 21 – 25 and 27 – 30 months) and only one participant at certain ages. Having more participants at every age would give more details about the development of the testability in this age group. Matching testability was also 100% by 26 months. This is younger than what is currently provided in the literature - the testability of matching LEA symbols was found to be only 75% in infants 36 months old.[86,90]

4) Face Cards and Patti Pics in a 2AFC format give equivalent VA to ETDRS in adult participants. This hypothesis was true for the Face cards, but not for the Patti Pics. The Face Cards gave equivalent VA to the ETDRS in the adult group, while the Patti Pics overestimated the VA by three lines on average. Subsequent to the study, we learned that in the commercially-available Patti Pics, all the symbols except the square are scaled 18% larger than the Snellen equivalent i.e. the widths of the lines were 18% wider. However, the Snellen principle was still maintained for the square, as for the other Patti Pics i.e. the width of the line is 20% of the size of the whole optotype (Ed Kopilansky, Precision Vision, personal communication). This was done because it was found empirically that the square was easier to see at threshold than the other shapes. The symbols used in our study were based on the actual Snellen equivalent (smaller than commercially available Patti Pics for the equivalent stated acuity level). So, this implies that, if the clinically available Patti Pics were used, the overestimation would be even greater.

An interesting finding was that recognition acuity was less developed than resolution VA at 18 months and developed more quickly so as to reach similar levels by about 36 months. This indicates that the two types of VA are not interchangeable. This has been previously shown for older participants,[24–29] but this is the first time this has been shown for infants of this age. This again indicates that a measure of recognition acuity that can be used at a younger age would be useful.

6.2 Limitations

One of the major limitations of this study was the sample size for the infants. This was the result of the difficulty in recruiting for the main infant study (16 – 42 months). Parents seemed less willing to have their child participate. For example, flyers were spread to a daycare facility of about 30 infants in our age group and no responses were received. It was particularly difficult to obtain data from all ages in our targets age group. This resulted in a small sample size with some gaps in the age distribution. In future studies, extensive advertising may be necessary to increase the number of participants enrolled and different study locations could be included. A second limitation was that the duration of each VA task was not recorded. Based on the examiner's observation, the 2AFC was quicker than the matching task for both the training and testability phase. If each task had been timed, quantitative evidence of this would be obtained. This would have provided a valuable tool to compare the different measures of

VA, in addition to passing the testability phase. Lastly, in our study, we only measured and compared the testability of the matching task and not the relative ability to obtain an actual VA threshold. It is possible that children may have been able to pass the testability, but not complete the whole VA routine. Measurement of VA would be of importance to compare to the 2AFC in terms of the difference in VA and duration of testing.

6.3 Conclusion

The Face Cards shows promise for measuring recognition acuity in infants and adults. The difficulty of the two-alternative forced choice method during the testability phase was found to be similar to the matching method in typically developed infants. Recognition acuity values increased with age over the infant range at a higher rate than resolution acuity. The results from adults indicate that the Face Cards is a valid recognition acuity test, giving similar VA to the ETDRS acuity, and that for an individual patient who can respond by pointing or looking after instruction or training, the Face test would give an accurate assessment of letter recognition acuity.

6.4 Future work

This thesis was done to establish a visual acuity test to measure recognition acuity that is suitable for infants. A study with a larger sample would give us valuable information on how the 2AFC method works in infants with different skills and mental abilities. Studying the 2AFC cards in special needs populations would also give valuable information about whether the testability with these cards is higher than other methods. We found that the 2AFC and the matching task have similar testability in the normal population, but a special needs child may perform differently. In addition, it would be worthwhile to test the usefulness of the Face Cards for detecting amblyopia and whether the face optotype performs like a crowded or uncrowded optotype in this condition.

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