Title: Preferential looking measures of grating acuity: development and applications

Running Title: Preferential Looking History & Application

Authors: Olivia Reed, B.S.*; D. Luisa Mayer, PhD§; T. Rowan Candy, PhD, FAAO*

Institutions:

* Indiana University School of Optometry, Bloomington, IN

§ New England College of Optometry, Harvard Medical School & Children's Hospital, Boston, MA

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Correspondence: Rowan Candy, 800 Atwater Avenue, Bloomington, IN 47405, 812-855-9340 rcandy@indiana.edu

Date of Submission: April 28, 2016

This review presents the challenges faced in the development of the preferential looking grating acuity approach to assessing the vision of young patients. The goal of the review is to provide the scientific rationale involved in the design of the Teller Acuity Cards and their application using the Acuity Card Procedure, to serve as an educational tool for users. Recent technological advances have also facilitated the development of new methods of visual acuity assessment that apply the principles of preferential looking. Scientists and developers can expect to address these same challenges in developing new methods.

Key Words: Preferential Looking, review, grating acuity, Teller Acuity Cards, infants

Part One: Background

In parallel with the potential for improved management of visual disorders in infancy, it is becoming increasingly important to develop efficient and affordable methods of functional visual assessment for non-verbal patients. Recent advances in technology provide an opportunity to transform the process of visual acuity measurement for young and non-verbal patients, particularly in methodologies based on the principles of preferential looking. Newly developed display technologies and eye tracking devices with high temporal and spatial resolution hold significant promise. (1, 2) The goal of this review is to provide clinicians and scientists with an educational tool that lays out the historical and scientific rationale behind preferential looking techniques and how they were translated from the laboratory to the clinic. It provides a resource for those first learning the technique and addresses issues that scientists and developers can expect to confront when designing novel equipment and clinical applications for preferential looking techniques.

Preferential looking techniques were borne out of a need to assess visual function in subjects unable to complete typical testing used for adults. The version used clinically to assess grating visual acuity merely requires the subject to indicate, by looking, an ability to discriminate spatial detail from a blank stimulus, precluding the need for an understanding of the task or a verbal response. For the current purposes, we will define grating visual acuity as the limit of a patient's ability to discriminate a black and white grating pattern of known spacing from a uniform, luminance-matched gray comparison stimulus (Figure 1). This limit is reached by making the grating progressively narrower (an increase in spatial frequency). It is important to note that, when compared in angular units, grating acuity tests tend to provide higher acuity estimates than typical recognition acuity tests in children and adults with visual abnormalities.(3-6) This difference is dependent upon the factors underlying the vision loss (e.g., the difference varies with type of amblyopia and the presence or absence of binocularity), and is thought to be largely due to differences in the stimuli (i.e., a simple grating vs. a complex pattern) and the task (i.e., resolution of a grating vs. recognition of the spatial relationships between resolved features). (6) While not directly equivalent to typical clinical estimates of recognition acuity, grating acuity has proven to be the most successful measure of acuity for younger infants and children for whom recognition methods are ineffective. (3, 7, 8)

Grating acuity assessment has also been achieved using other techniques, such as the visually-evoked potential (VEP) or optokinetic nystagmus (OKN) paradigms. Infants' fixations of grating targets can be recorded and interpreted using either behavioral assessments of their gaze responses or the resulting electroencephalogram generated in early visual cortex. While the VEP has proven effective in the assessment of grating acuity (9-11), the financial investment and significant expertise required for its use have limited its practicality for the typical clinical practice.(12)

Fantz's Preferential Looking Technique

Robert Fantz developed the original preferential looking technique for assessing visual function in infants. (13) He compared their gaze preferences for viewing a simultaneously presented black and white grating and a luminancematched grey square, capitalizing on infants' intrinsic preference for viewing the grating pattern rather than the blank stimulus. (14) The stimuli were presented beside each other for a specified period of time in two trials, with the location of the grating changed between trials to minimize the effect of bias for viewing to the left or right. During the trial, the observer's task was to monitor the infant's fixation behavior through a peephole centered between the two stimulus positions to judge which stimulus the infant was looking at. Fixation times for both the grating pattern and the grey target were then summed over the two presentations, with their acuity was defined as the finest grating that they fixated at least 75% of the time.

One significant limitation of this technique is that the result will vary depending on the metric selected for the analysis. For example Fantz et al. (1962) found that total looking time and mean length of fixation demonstrated fixation preference, while the number of individual fixations did not. (14) Further, infants' responses may vary as they habituate to the grating stimulus following multiple presentations. (15)

Teller's Forced-Choice Preferential Looking (FPL)

Davida Teller and her colleagues refined the preferential looking technique to create the forced-choice preferential looking method of grating acuity assessment. (16, 17) The approach was designed to provide an objective psychophysical method to assess infant vision in a laboratory setting. Forced-choice preferential looking is a variation on the classical psychophysical two-alternative forced-choice (2AFC) paradigm, with the setup being very similar to that of Fantz's technique. In forced-choice preferential looking, however, the observer is tasked with identifying where the grating pattern is located, to the left or right, rather than recording the infant's looking behavior. This approach allows the observer to integrate all aspects of the infant's behavior (e.g., speed of fixation shift, time spent fixating the target, facial expression, etc.) to make a judgment of grating location, rather than relying on a single metric to determine preference. The observer's percentage correct for each grating width is then calculated and, if their performance is significantly greater than chance (i.e., 50% correct for a two alternative procedure), it can be inferred that the infant detected the grating, assuming no other extraneous cues to grating location are present. The infant's acuity is defined as the finest grating for which the observer's performance is significantly greater than chance.

Forced-choice preferential looking has been used to gain an understanding of a wide range of visual functions including color vision, (18) spectral sensitivity (19) stereopsis and fusion,(20) vernier acuity(21) and contrast sensitivity.(22) In two-alternative forced-choice procedures, threshold is often defined as the stimulus level (in this case spatial frequency of the grating) at which the observer performs at a pre-determined percentage greater than chance (e.g., 75% correct). This calculation requires that a curve be fit to the data. Variance in the data, the

number of stimulus levels tested, and the number of judgments greatly influence confidence in the estimate, and one hundred or more trials may be required to achieve a reliable threshold, which is impractical in clinical settings. (23)

While it is possible to obtain acuity estimates from infants and young children using forced-choice preferential looking employing a reward for detecting the grating (a variant of the procedure known as operant preferential looking), success rates can be low, particularly in the 18-24 month age range. (7, 24) Therefore, it became clear that modifications to the procedure would need to be made to increase the clinical utility of the technique.

"Fast" Forced-Choice Preferential Looking

Some of the first steps taken to modify the forced-choice preferential looking procedure involved reducing the time required to perform the test by reducing the number of trials required to achieve statistical reliability of the threshold measurement. Held et al. (1979) developed a quick method based on the theory that infants prefer to fixate blank fields when the spatial frequency (SF) of the grating reaches near-threshold levels. (25) This method produced acuity estimates for infants aged 2 to 52 weeks in less than five minutes. (26) While the method successfully addressed the time constraints of FPL, its repeatability was not adequate to provide reliable threshold estimates. (27, 28)

Mayer and colleagues approached the time constraint by utilizing a staircase procedure. The grating SFs tested depended upon the observer's prior performance: if on two trials of a given SF the right/left location on both trials was identified correctly, SF was increased, if one of two trials was judged incorrectly, SF was decreased., This enabled faster estimation of the individual's threshold. This procedure could assess the child's acuity in 20 to 25 trials, with an 85% successful completion rate. (29) However, it was limited in its application due to its susceptibility to variability(23) and the fact that it required up to 20 minutes to obtain an acuity measure for each eye, which is still too lengthy for the constraints of the typical eye examination.(29) Additional studies have employed more complex staircase paradigms to minimise variability.(30)

Another approach to reducing the variability arising from small numbers of trials was the diagnostic grating procedure proposed by Velma Dobson. This procedure utilized a grating that had proven detectable by 95% of infants with normal visual acuity at a given age. The observer began with a grating of low spatial frequency, followed by the 'diagnostic grating.' The low spatial frequency grating was used to detect gross deficits in visual performance, while the diagnostic grating allowed for comparison to age norms. Performance for these gratings can inform further testing, during which acuity measures can be further refined. (31, 32)

The Acuity Card Procedure

Due to the limitations of forced-choice preferential looking procedures, Teller and colleagues developed a new approach to grating acuity measurement for clinical applications, which they named the acuity card procedure (ACP). In this procedure, a single observer conducts the test using subjective judgments of the infant's ability to detect a grating pattern presented on an individual rectangular card. The observer controls all aspects of testing: selecting the progression of the cards, presenting the gratings as many times as necessary, and judging the infant's behaviors to determine whether the grating was resolved. Detailed descriptions of the ACP can be found in McDonald et al. (1985) and Teller (1986) and in the Teller Acuity Card Handbook.(33-35) A video of one of the authors performing the ACP with Teller Acuity Cards can be found online^a.

This modification permitted preferential looking to be moved forward into full development as a clinical test and implemented by a number of groups beyond Teller and Dobson and their colleagues.(26, 30, 36-38) Other tests have since been developed using this basic testing principle, such as the Keeler Acuity Cards(39), City-Cardiff Acuity Test, the Cardiff Acuity Cards(40) and the Pacific Acuity Test.(41) Notably, Jones and colleagues (2015) suggest that the acuity card procedure and other similar clinical tests may be optimal for testing thresholds as infant lapses in attention can be accommodated during testing and because the resulting guessing rate is low.(42)

Part Two - Normative Data

Clinical tests of acuity for infants and young children require normative data collected at the relevant ages. These data are needed to determine if a patient's acuity is within or outside the normal limits for their age. The need for new normative data must be addressed for each new version of a clinical test.

^a https://vimeo.com/100417709

Preliminary acuity card procedure norms and the test-retest reliability of binocular and monocular grating acuities using prototype acuity cards were obtained from infants ages 1-12 months and children ages 18-26 months.(43, 44) Importantly, these normative ACP data agreed with forced-choice preferential looking in visually normal subjects and in infants with ocular disorders.(8, 43, 44) A commercial version of the acuity cards, called Teller Acuity Cards (TAC), was produced following these initial validation studies, and these cards have been modified somewhat since then with a different manufacturing process, becoming the TACII. The TAC and TAC II were specifically designed to be used with the ACP and the success rate in using this testing combination with young subjects is high, as discussed by Teller and colleagues.(34)

In translating these tests into clinical application, care must be taken in their manufacture to ensure that there are no artefacts in the printing process that could provide a cue to the grating location. These could draw a patient's attention to a grating that they cannot actually resolve. For example, particular care must be taken in looking for 'edge artefacts' at the border of the grating.(39, 45) One goal of the defined border mask in the Keeler Acuity Test was to avoid this potential problem.

Large-scale age norm studies of grating acuity measured with the original TACs were performed by three groups. Courage and colleagues measured binocular acuity in 140 children between birth and 36 months,(46) Mayer and colleagues measured monocular acuities and interocular acuity differences in 460 children between 1 month and 48 months,(47) and Salamao and Ventura obtained binocular and monocular TAC acuities in 646 children between birth and 36 months.(48) These three normative data sets provided the norms published with the Teller Acuity Cards.(35) A number of other studies showed that TAC normative values tend to be higher than normative data collected with the later TAC II cards, by approximately 0.3 to 0.5 octaves, particularly for older children.(49-52)

Part Three - Clinical Applications and Methodologies

Once normative values have been established, scientists and clinicians must determine how to use them effectively to detect, diagnose and monitor a range of clinical conditions. Important components of these topics are reviewed below.

Test-retest reliability and predictive validity

Test-retest reliability must be evaluated to determine whether a change in a patient's acuity obtained by the same or a different tester is within expected limits. Comparison of the between tester differences for visually normal children and children with ocular abnormalities tested with the same TAC procedure is instructive. In the study of normative monocular acuity, Mayer and colleagues (1995) found that 90% of between tester differences were 0.5 octave or less and 98% were 1.0 octave or less.(47) Between tester reliability was somewhat lower for infants of 1 to 12 months compared with ages 18-48 months. Birch and Hale also found greater test-retest differences in visually normal 1 month olds.(53) Getz and colleagues (1999) studying a clinical population with the same TAC procedure,

found monocular test-retest differences of 0.5 octave^b or less in 79%, and 1.0 octave or less in 95% of children without ocular complications, while for the children with ocular disorders, test-retest differences of 0.5 octave or less were found for 78% and 1.0 octave or less in 91%. There was no difference in test-retest differences for children as a function of their acuity.(54)

Studies of children with severe neurological problems affecting vision, motor function and cognition found reduced between tester reliability in binocular TAC acuities: differences of less than or equal to 1.0 octave occurred for 79-86% of tests of children with cerebral palsy,(55) and for 75% of tests of children with cortical visual impairment.(56)

In combination, these studies suggest that a 1.5 octave or larger decrement in TAC acuity should be considered clinically significant and suggestive of a real acuity difference in most patients. These data define the ability of the technique to detect changes in acuity.

Interocular difference in grating acuity is important for evaluating monocular abnormalities. Birch & Hale (1988) analyzed different criteria for judging the presence or absence of amblyopia based on normative data from their large study of forced-choice preferential looking grating acuities in visually normal infants. Applied to a clinical population at risk for monocular deprivation amblyopia, the interocular difference was more sensitive (detected amblyopia correctly) than

^b An octave corresponds to a doubling or halving of the SF of the grating. For example, if the expected threshold for a given age group is 60 cycles/degree, the observer may begin with a card of spatial frequency 15 cycles/degree, which represents 2 octaves above the expected threshold. This notation is used due to its compatibility with the logarithmic scale of visual acuity measurements (e.g., logMAR acuity).

criteria based on absolute acuity, while specificity (correctly identifying the absence of amblyopia) was equivalent for all criteria.(53) However, it should be noted that deprivation amblyopia is a severe, and rare, form of amblyopia; therefore, results from studies of deprivation amblyopia cannot be assumed to apply to refractive or strabismic amblyopia.

Mash and Dobson (1998) assessed the predictive validity of TAC grating acuity in infants at risk of visual impairment in a neonatal intensive care unit. These children were followed up to age 4 years. Normal grating acuity at the early age was predictive of normal grating acuity and recognition acuity later in life for 73-95% of eyes tested. Grating acuities below normal at the early age were predictive of low grating acuity in somewhat fewer eyes (39-80%).(57) Hall and colleagues (2000) reported similar findings for the predictive validity of grating acuity in infants at risk for abnormal development, suggesting that a normal TAC acuity is more predictive than an abnormal TAC acuity in this population. (58)

Grating acuity in ocular and vision disorders

In disorders of the retina and optic nerve, grating acuity deficits are associated with the type and severity of the disorder. Dobson and colleagues (1995) found that grating acuity varied in relation to the type and severity of retinal residua in infants weighing less than 1251 grams at birth who developed retinopathy of prematurity. (59) Weiss and Kelly (2003) found in children with bilateral optic nerve hypoplasia, early acuity expressed as the deficit relative to normal acuity for age was significantly correlated with outcome acuity, and together with optic disc diameter accounted for 73% of the variance in acuity outcome.(60)

In children with infantile nystagmus with various etiologies, early grating acuities and maturation of grating acuity vary between the different disorders. Fu and colleagues (2011) studied a large sample of children with infantile nystagmus categorized into four groups - idiopathic, albinism, optic nerve hypoplasia, and retinal disorders- finding variation in the average grating acuity under age 24 months, with different maturation of acuity with age for the four groups.(61)

These studies demonstrate that grating visual acuities in young children with structural ocular disorders are measureable, show reductions corresponding in general with the severity of the disorder, and may mature with unique time courses. The latter may partially explain the lower predictive validity of early measures of grating acuity in the at-risk populations described above.(57, 58) Prediction may be better for specific disorders(62, 63) and improved by considering the structural features of the disorder, for example in retinopathy of prematurity and optic nerve hypoplasia.(59, 60)

TACs have proven useful in the assessment of vision in children with cerebral (or cortical) visual impairment, in whom abnormal visual behaviors cannot be explained by optical or ocular causes. In these cases, grating acuity deficit indicates the severity of visual impairment, although other visual functions – perceptual, spatial, and attentional - may be impaired independently of acuity. (64-66) This is not surprising given the spectrum of brain injury and the heterogeneity of clinical manifestations.(65) Grating acuity deficits (relative to mean normal acuity for age)

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correlated significantly with grating acuity deficits up to 3 to 6 years later,(62) suggesting some stability of the grating acuity deficit in cerebral visual impairment. Thus, in this condition, perhaps the most challenging pediatric vision disorder to assess clinically, grating acuity can provide a relatively stable measure that can be obtained throughout infancy and childhood.

Grating acuities are also useful in assessing children with cerebral palsy. The acuities vary with the severity of motor and mental impairment in these children(55, 67) and in relation to the severity of cerebral lesions.(68, 69) This is consistent with the conclusion that the more severely neurologically impaired children are most likely to have cortical/cerebral visual impairment.(69, 70) A high proportion of children with cerebral palsy also have refractive errors and oculomotor abnormalities (70), which must both be considered during testing. Children with cerebral palsy and cerebral visual impairment pose difficult examination challenges and grating acuity forms a component of their assessment.

Amblyopia

Management of amblyopia is a significant part of pediatric clinical practice. Grating acuity has been used to indicate a monocular acuity deficit in one eye of a child presenting with a risk factor for amblyopia, such as strabismus, anisometropia, or monocular cataract. Two studies found that in esotropic children with a clinically defined fixation preference, grating acuity was not significantly reduced in the nonpreferred eye.(71, 72) The relationship between these two assessments of visual function needs to be further understood.(73) These results suggested that grating acuity is not sensitive to strabismic amblyopia as defined by a fixation preference for one eye. However, grating acuity relative to normal monocular acuity for age, was shown to be sensitive to various types of amblyopia defined by reduced optotype acuity.(74) Grating acuity changes were also associated with changes in fixation preference in esotropic children following patching therapy for deprivation amblyopia due to cataracts.(75)

Grating acuity has been used to study the effects of surgery for monocular and binocular congenital cataracts on visual development(63, 76, 77) and to determine the efficacy of occlusion therapy for deprivation amblyopia.(78-80) Together these studies indicate that grating acuities have a place in the assessment of congenital cataracts and in the assessment of patching for amblyopia in strabismic and deprivation amblyopia.

Clinical Challenges

Clinical populations present a number of methodological challenges. For example, when testing an individual with horizontal nystagmus it can be difficult to determine whether changes in horizontal gaze position are the result of grating detection or are due to the nystagmus. Orienting the TAC vertically(61) allows the tester to judge the patient's detection of the grating using vertical eye movements.

The interpretation of grating acuities in patients with macular degeneration or other foveal abnormalities can also be problematic. These patients have significant discrepancies between grating and recognition acuity, typically with better grating than recognition acuity. (3, 81) This can be explained, in part, by the

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large sis of the grating stimulus and the repetitive stimulus elements, which may enable the patient with a central scotoma to detect the grating with peripheral retina. For these patients, grating acuity can be useful in addition to recognition acuity testing, as each method provides unique information about the depth and nature of the visual deficit.(81)

Other concerns include the impact of testing distance for patients with high refractive errors, accommodative dysfunction or aphakia. The TAC manual suggests appropriate testing distances for different ages.(35) Patients with limited acuity or aphakia may require an adjusted distance, which requires additional consideration of their optical focus (an uncorrected myope may be focused only at near distances, or a patient with an IOL may only have one focused distance, for example). The visual angle separating the center of the acuity card and the grating stimulus changes with viewing distance, so the stimulation of different sections of peripheral retina should also be considered when modifying viewing distance. Knowledge of distributions of refractive error associated with particular conditions (e.g., Down syndrome or albinism) and accommodative status help inform the distance decision. When a non-standard testing distance is used, the observer must convert the spatial frequency before comparing the results to normative data.

Other designs

Other grating acuity tests have been developed based on the forced-choice preferential looking principle. For example, the Keeler Acuity Cards for Infants (Keeler) and the City-Cardiff Acuity Test (Haag-Streit) use round grating patches with a masking border rather than the squares of the TAC. The Cardiff Acuity Cards (Good-Lite & Richmond Products) use outlines of objects to make the test more interesting for young children(40), and the Pacific Acuity Test (Good-Lite) combines this outline, or vanishing optotype, approach into a test of both recognition and resolution acuities for toddlers.(41) Despite differences in stimuli, the acuities obtained with these tests have not been shown to differ dramatically from TAC acuities. (38, 82-84) Two additional tests, Lea Grating Acuity Test (Good-Lite) and Patti Stripes Square Wave Grating Paddles (Precision Vision) use gratings on paddles to be held up next to a uniform gray paddle.

With current advances in technology, a fully automated, computerized method of assessing grating acuity is becoming increasingly feasible. There are a number of these systems in development. (1, 2, 85) Sturm and colleagues (2011) developed a gaze-tracking method to make an objective measure of grating acuity. The system measures the relative fixation time for the grating pattern and employs a statistical algorithm to determine if the grating was discriminated. Preliminary tests in adults have been completed(85) and a subsequent study by Hathibelagal and colleagues (2015) has tested infants. However, a human observer used the gaze data to judge detection of the gratings in the infant study.(2)

Jones and colleagues (2014) also developed a fully automated eye-tracking system for measuring grating acuity (ACTIVE). The ACTIVE method utilizes a sinewave grating pattern presented on a luminance-matched background. The spatial frequency of the grating is determined using an adaptive staircase paradigm. Preliminary tests in infants aged 2 to 12 months have produced grating acuities in line with TAC norms, with reasonable repeatability. (1)

The potential benefits of these video-based and gaze-tracking methodologies are significant. They could provide a more objective measure of acuity, avoid the problems of observer training and reliability, and reduce testing time. They can also be modified for the assessment of other visual functions. Potential challenges include cost and portability (although the advent of commercial tablet devices reduces the cost of digital presentation significantly(86)), display calibration, and the classical question of gaze parameters (e.g. duration, repetition, speed) to include in the calculation. Other considerations include the difficulty of using eye tracking in individuals with abnormal saccades(87), nystagmus, those with fleeting attention, and in children with cerebral visual impairment. While these methods present a more objective measure of acuity, they will need to replicate the skill of a clinician or trained tester in interpreting responses, to the point that they result in consistent norms and can meet the challenges discussed above in clinical testing. Additionally, developers should consider the age range for which their test is intended. Acuity develops rapidly in younger populations and it is critical that the stimulus spatial frequency ranges are suitable for the entire intended population. The stimulus must also be capable of holding the patient's attention to achieve success and it is advisable to test this in toddlers, an age when success tends to be lowest.

Summary

In summary, although variable relative to estimates of recognition acuity in adults, grating visual acuity can be used for the assessment of acuity in young and non-verbal patients with a number of ocular disorders. The TAC and similar stimuli have been modified specifically for clinical settings such that equipment is simple and only one examiner is required. The saliency and attentional difficulties of testing young children beyond infancy make preferential looking methods challenging in testing toddlers. Other tests have therefore been developed to transition from the limited behavioral repertoire of infants into the recognition testing completed with adult subjects.

With the current exciting advances in display and camera technology, the use of grating acuity testing has the potential to increase, providing further understanding of visual function in a wide range of populations. The challenges faced in the early development of the TAC, from a laboratory based psychophysical paradigm to a practical clinical test, will also apply to these new approaches.

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ACKNOWLEDGEMENTS/COI:

The Teller Acuity Cards® (TAC) were developed by Davida Teller, PhD and Velma Dobson, PhD. The TAC Handbook was prepared by Drs. Teller and Dobson, and Drs. Candy & Mayer contributed to revisions of the Handbook. The Teller Acuity Cards® are the registered trademark of the University of Washington and are produced under license from the University of Washington by Stereo Optical Company, Inc. The University of Washington, CoMotion, supported the preparation of this manuscript, to synthesize and summarize clinical and research studies of these techniques in pediatric use for clinical and research purposes.

References

1. Jones PR, Kalwarowsky S, Atkinson J, Braddick OJ, Nardini M. Automated measurement of resolution acuity in infants using remote eye-tracking. Investigative ophthalmology & visual science. 2014;55(12):8102-10.

2. Hathibelagal AR, Leat SJ, Irving EL, Nandakumar K, Eizenman M. Measuring Infant Visual Acuity with Gaze Tracker Monitored Visual Fixation. Optometry and vision science : official publication of the American Academy of Optometry. 2015.

3. Mayer DL, Fulton AB, Rodier D. Grating and recognition acuities of pediatric patients. Ophthalmology. 1984;91(8):947-53.

4. Stiers P, Vanderkelen R, Vandenbussche E. Optotype and grating visual acuity in patients with ocular and cerebral visual impairment. Investigative ophthalmology & visual science. 2004;45(12):4333-9.

5. Dobson V, Quinn GE, Tung B, Palmer EA, Reynolds JD. Comparison of recognition and grating acuities in very-low-birth-weight children with and without retinal residua of retinopathy of prematurity. Cryotherapy for Retinopathy of Prematurity Cooperative Group. Investigative ophthalmology & visual science. 1995;36(3):692-702.

6. McKee SP, Levi DM, Movshon JA. The pattern of visual deficits in amblyopia. Journal of vision. 2003;3(5):380-405.

7. Mayer DL, Dobson V. Visual acuity development in infants and young children, as assessed by operant preferential looking. Vision research. 1982;22(9):1141-51.

8. Preston KL, McDonald M, Sebris SL, Dobson V, Teller DY. Validation of the acuity card procedure for assessment of infants with ocular disorders. Ophthalmology. 1987;94(6):644-53.

9. Norcia AM, Tyler CW. Spatial frequency sweep VEP: visual acuity during the first year of life. Vision research. 1985;25(10):1399-408.

10. Sokol S, Moskowitz A, McCormack G. Infant VEP and preferential looking acuity measured with phase alternating gratings. Investigative ophthalmology & visual science. 1992;33(11):3156-61.

11. Skoczenski AM, Norcia AM. Development of VEP Vernier acuity and grating acuity in human infants. Investigative ophthalmology & visual science. 1999;40(10):2411-7.

12. Guidelines ICfPCE, Fulton AB, Brecelj J, Lorenz B, Moskowitz A, Thompson D, et al. Pediatric clinical visual electrophysiology: a survey of actual practice. Documenta ophthalmologica Advances in ophthalmology. 2006;113(3):193-204.

13. Fantz RL. Visual perception from birth as shown by pattern selectivity. Annals of the New York Academy of Sciences. 1965;118(21):793-814.

14. Fantz RL, Ordy JM, Udelf MS. Maturation of Pattern Vision in Infants during First 6 Months. J Comp Physiol Psych. 1962;55(6):907-&.

15. Colombo J, Mitchell DW. Infant visual habituation. Neurobiology of learning and memory. 2009;92(2):225-34.

16. Teller DY, Morse R, Borton R, Regal D. Visual acuity for vertical and diagonal gratings in human infants. Vision research. 1974;14(12):1433-9.

17. Teller DY. Forced-Choice Preferential Looking Procedure - Psychophysical Technique for Use with Human Infants. Infant Behav Dev. 1979;2(2):135-53.

18. Teller DY, Peeples DR, Sekel M. Discrimination of chromatic from white light by two-month-old human infants. Vision research. 1978;18(1):41-8.

19. Pulos E, Teller DY, Buck SL. Infant color vision: a search for shortwavelength-sensitive mechanisms by means of chromatic adaptation. Vision research. 1980;20(6):485-93.

20. Birch EE, Shimojo S, Held R. Preferential-looking assessment of fusion and stereopsis in infants aged 1-6 months. Investigative ophthalmology & visual science. 1985;26(3):366-70.

21. Manny RE, Klein SA. The development of vernier acuity in infants. Current eye research. 1984;3(3):453-62.

Atkinson J, Braddick O, Moar K. Development of contrast sensitivity over the first 3 months of life in the human infant. Vision research. 1977;17(9):1037-44.
McKee SP, Klein SA, Teller DY, Statistical properties of forced-choice

psychometric functions: implications of probit analysis. Perception & psychophysics. 1985;37(4):286-98.

24. Shute R, Candy R, Westall C, Woodhouse JM. Success rates in testing monocular acuity and stereopsis in infants and young children. Ophthalmic & physiological optics : the journal of the British College of Ophthalmic Opticians. 1990;10(2):133-6.

25. Held R, Gwiazda J, Brill S, Mohindra I, Wolfe J. Infant visual acuity is underestimated because near threshold gratings are not preferentially fixated. Vision research. 1979;19(12):1377-9.

26. Gwiazda J, Wolfe JM, Brill S, Mohindra I, Held R. Quick assessment of preferential looking acuity in infants. American journal of optometry and physiological optics. 1980;57(7):420-7.

27. Banks MS, Stephens BR, Dannemiller JL. A failure to observe negative preference in infant acuity testing. Vision research. 1982;22(8):1025-31.

28. Teller DY, Mayer DL, Makous WL, Allen JL. Do preferential looking techniques underestimate infant visual acuity? Vision research. 1982;22(8):1017-24.

29. Mayer DL, Fulton AB, Hansen RM. Preferential looking acuity obtained with a staircase procedure in pediatric patients. Investigative ophthalmology & visual science. 1982;23(4):538-43.

30. Lewis TL, Maurer D. Preferential looking as a measure of visual resolution in infants and toddlers: a comparison of psychophysical methods. Child development. 1986;57(4):1062-75.

31. Dobson V. Clinical applications of preferential looking measures of visual acuity. Behavioural brain research. 1983;10(1):25-38.

32. Dobson V, Teller DY, Lee CP, Wade B. A behavioral method for efficient screening of visual acuity in young infants. I. Preliminary laboratory development. Investigative ophthalmology & visual science. 1978;17(12):1142-50.

33. McDonald MA, Dobson V, Sebris SL, Baitch L, Varner D, Teller DY. The acuity card procedure: a rapid test of infant acuity. Investigative ophthalmology & visual science. 1985;26(8):1158-62.

34. Teller DY, McDonald MA, Preston K, Sebris SL, Dobson V. Assessment of visual acuity in infants and children: the acuity card procedure. Developmental medicine and child neurology. 1986;28(6):779-89.

35. Dobson V. Teller Acuity Card II Reference and Instruction Manual Chicago, IL: Stereo Optical; 2009. Available from: <u>http://www.stereooptical.com/wp-</u> <u>content/uploads/2013/10/TACII-Manual-Appendices.pdf</u>.

36. Atkinson J, Braddick O, Pimm-Smith E. 'Preferential looking' for monocular and binocular acuity testing of infants. The British journal of ophthalmology. 1982;66(4):264-8.

37. Mohn G, van Hof-van Duin J. Rapid Assessment of Visual Acuity in Infants and Children in a Clinical Setting, Using Acuity Cards. In: Jay B, editor. Detection and Measurement of Visual Impairment in Pre-Verbal Children. Documenta Ophthalmologica Proceedings Series. 45: Springer Netherlands; 1986. p. 363-71.

38. Neu B, Sireteanu R. Monocular acuity in preschool children: Assessment with the Teller and Keeler acuity cards in comparison to the C-test. Strabismus. 1997;5(4):185-202.

39. Robinson J, Moseley MJ, Fielder AR. Grating acuity cards - spurious resolution and the 'edge artefact'. Clin Vision Sci. 1988;3(4):285-8.

40. Adoh TO, Woodhouse JM. The Cardiff acuity test used for measuring visual acuity development in toddlers. Vision research. 1994;34(4):555-60.

41. Lowery JP, Hayes JR, Sis M, Griffith A, Taylor D. Pacific acuity test: testability, validity, and interobserver reliability. Optometry and vision science : official publication of the American Academy of Optometry. 2014;91(1):76-85.

42. Jones PR, Kalwarowsky S, Braddick OJ, Atkinson J, Nardini M. Optimizing the rapid measurement of detection thresholds in infants. Journal of vision. 2015;15(11):2.

43. McDonald M, Ankrum C, Preston K, Sebris SL, Dobson V. Monocular and binocular acuity estimation in 18- to 36-month-olds: acuity card results. American journal of optometry and physiological optics. 1986;63(3):181-6.

44. McDonald M, Sebris SL, Mohn G, Teller DY, Dobson V. Monocular acuity in normal infants: the acuity card procedure. American journal of optometry and physiological optics. 1986;63(2):127-34.

45. Hainline L, Evelyn L, Abramov I. Acuity cards—what do they measure? Investigative Ophthalmology and Visual Science (Suppl). 1989;30:310.

46. Courage ML, Adams RJ. Visual acuity assessment from birth to three years using the acuity card procedure: cross-sectional and longitudinal samples. Optometry and vision science : official publication of the American Academy of Optometry. 1990;67(9):713-8.

47. Mayer DL, Beiser AS, Warner AF, Pratt EM, Raye KN, Lang JM. Monocular acuity norms for the Teller Acuity Cards between ages one month and four years. Investigative ophthalmology & visual science. 1995;36(3):671-85.

48. Salomao SR, Ventura DF. Large sample population age norms for visual acuities obtained with Vistech-Teller Acuity Cards. Investigative ophthalmology & visual science. 1995;36(3):657-70.

49. Clifford CE, Haynes BM, Dobson V. Are norms based on the original Teller Acuity Cards appropriate for use with the new Teller Acuity Cards II? Journal of

AAPOS : the official publication of the American Association for Pediatric Ophthalmology and Strabismus / American Association for Pediatric Ophthalmology and Strabismus. 2005;9(5):475-9.

50. Leone JF, Mitchell P, Kifley A, Rose KA, Sydney Childhood Eye S. Normative visual acuity in infants and preschool-aged children in Sydney. Acta ophthalmologica. 2014;92(7):e521-9.

51. Qiu Y, Li XQ, Yan XM. [Evaluation of grating visual acuity development in normal infants]. [Zhonghua yan ke za zhi] Chinese journal of ophthalmology. 2011;47(11):995-1000.

52. Kasugai M, Asano N, Hori H, Sakurai H, Kawase Y. Comparison between Teller Acuity Cards and Teller Acuity Cards II. Journal of Japanese Association of Certified Orthoptist. 2006;35:141-6.

53. Birch EE, Hale LA. Criteria for monocular acuity deficit in infancy and early childhood. Investigative ophthalmology & visual science. 1988;29(4):636-43.

54. Getz LM, Dobson V, Luna B, Mash C. Interobserver reliability of the Teller Acuity Card procedure in pediatric patients. Investigative ophthalmology & visual science. 1996;37(1):180-7.

55. Hertz BG, Rosenberg J. Effect of mental retardation and motor disability on testing with visual acuity cards. Developmental medicine and child neurology. 1992;34(2):115-22.

56. Hertz BG, Rosenberg J, Sjo O, Warburg M. Acuity card testing of patients with cerebral visual impairment. Developmental medicine and child neurology. 1988;30(5):632-7.

57. Mash C, Dobson V. Long-term reliability and predictive validity of the Teller Acuity Card procedure. Vision research. 1998;38(4):619-26.

58. Hall HL, Courage ML, Adams RJ. The predictive utility of the Teller acuity cards for assessing visual outcome in children with preterm birth and associated perinatal risks. Vision research. 2000;40(15):2067-76.

59. Dobson V, Quinn GE, Saunders RA, Spencer R, Davis BR, Risser J, et al. Grating visual acuity in eyes with retinal residua of retinopathy of prematurity. The Cryotherapy for Retinopathy of Prematurity Cooperative Group. Archives of ophthalmology. 1995;113(9):1172-7.

60. Weiss AH, Kelly JP. Acuity, ophthalmoscopy, and visually evoked potentials in the prediction of visual outcome in infants with bilateral optic nerve hypoplasia. Journal of AAPOS : the official publication of the American Association for Pediatric Ophthalmology and Strabismus / American Association for Pediatric Ophthalmology and Strabismus. 2003;7(2):108-15.

61. Fu VL, Bilonick RA, Felius J, Hertle RW, Birch EE. Visual acuity development of children with infantile nystagmus syndrome. Investigative ophthalmology & visual science. 2011;52(3):1404-11.

62. Birch EE, Bane MC. Forced-choice preferential looking acuity of children with cortical visual impairment. Developmental medicine and child neurology. 1991;33(8):722-9.

63. Birch EE, Subramanian V, Patel CC, Stager D, Jr. Preoperative visual acuity and contrast sensitivity in children with small, partial, or non-central cataracts. Journal of AAPOS : the official publication of the American Association for Pediatric Ophthalmology and Strabismus / American Association for Pediatric Ophthalmology and Strabismus. 2013;17(4):357-62.

64. Atkinson J, Braddick O. Visual and visuocognitive development in children born very prematurely. Progress in brain research. 2007;164:123-49.

65. Fazzi E, Signorini SG, Bova SM, La Piana R, Ondei P, Bertone C, et al. Spectrum of visual disorders in children with cerebral visual impairment. Journal of child neurology. 2007;22(3):294-301.

66. Ricci D, Anker S, Cowan F, Pane M, Gallini F, Luciano R, et al. Thalamic atrophy in infants with PVL and cerebral visual impairment. Early human development. 2006;82(9):591-5.

67. Costa MF, Ventura DF. Visual impairment in children with spastic cerebral palsy measured by psychophysical and electrophysiological grating acuity tests. Developmental neurorehabilitation. 2012;15(6):414-24.

68. Ipata AE, Cioni G, Bottai P, Fazzi B, Canapicchi R, Van Hof-Van Duin J. Acuity card testing in children with cerebral palsy related to magnetic resonance images, mental levels and motor abilities. Brain & development. 1994;16(3):195-203.

69. Schenk-Rootlieb AJ, van Nieuwenhuizen O, van Waes PF, van der Graaf Y. Cerebral visual impairment in cerebral palsy: relation to structural abnormalities of the cerebrum. Neuropediatrics. 1994;25(2):68-72.

70. Fazzi E, Signorini SG, R LAP, Bertone C, Misefari W, Galli J, et al. Neuroophthalmological disorders in cerebral palsy: ophthalmological, oculomotor, and visual aspects. Developmental medicine and child neurology. 2012;54(8):730-6.

71. Mayer DL, Fulton AB. Preferential looking grating acuities of infants at risk of amblyopia. Transactions of the ophthalmological societies of the United Kingdom. 1985;104 (Pt 8):903-11.

72. Ellis GS, Jr., Hartmann EE, Love A, May JG, Morgan KS. Teller acuity cards versus clinical judgment in the diagnosis of amblyopia with strabismus. Ophthalmology. 1988;95(6):788-91.

73. Cotter SA, Tarczy-Hornoch K, Song E, Lin J, Borchert M, Azen SP, et al. Fixation preference and visual acuity testing in a population-based cohort of preschool children with amblyopia risk factors. Ophthalmology. 2009;116(1):145-53.

74. Drover JR, Wyatt LM, Stager DR, Birch EE. The teller acuity cards are effective in detecting amblyopia. Optometry and vision science : official publication of the American Academy of Optometry. 2009;86(6):755-9.

75. Birch EE, Stager DR, Berry P, Everett ME. Prospective assessment of acuity and stereopsis in amblyopic infantile esotropes following early surgery. Investigative ophthalmology & visual science. 1990;31(4):758-65.

76. Birch EE, Swanson WH, Stager DR, Woody M, Everett M. Outcome after very early treatment of dense congenital unilateral cataract. Investigative ophthalmology & visual science. 1993;34(13):3687-99.

77. Lewis TL, Maurer D, Brent HP. Development of grating acuity in children treated for unilateral or bilateral congenital cataract. Investigative ophthalmology & visual science. 1995;36(10):2080-95.

78. Drews-Botsch CD, Celano M, Kruger S, Hartmann EE, Infant Aphakia Treatment S. Adherence to occlusion therapy in the first six months of follow-up and visual acuity among participants in the Infant Aphakia Treatment Study (IATS). Investigative ophthalmology & visual science. 2012;53(7):3368-75.

79. Lloyd IC, Dowler JG, Kriss A, Speedwell L, Thompson DA, Russell-Eggitt I, et al. Modulation of amblyopia therapy following early surgery for unilateral congenital cataracts. The British journal of ophthalmology. 1995;79(9):802-6.

80. Mayer DL, Moore B, Robb RM. Assessment of vision and amblyopia by preferential looking tests after early surgery for unilateral congenital cataracts. Journal of pediatric ophthalmology and strabismus. 1989;26(2):61-8.

81. White JM, Loshin DS. Grating acuity overestimates Snellen acuity in patients with age-related maculopathy. Optometry and vision science : official publication of the American Academy of Optometry. 1989;66(11):751-5.

82. Mackie RT, Saunders KJ, Day RE, Dutton GN, McCulloch DL. Visual acuity assessment of children with neurological impairment using grating and vanishing optotype acuity cards. Acta ophthalmologica Scandinavica. 1996;74(5):483-7.

83. Johnson C, Kran BS, Deng L, Mayer DL. Teller II and Cardiff Acuity testing in a school-age deafblind population. Optometry and vision science : official publication of the American Academy of Optometry. 2009;86(3):188-95.

84. Sharma P, Bairagi D, Sachdeva MM, Kaur K, Khokhar S, Saxena R. Comparative evaluation of Teller and Cardiff acuity tests in normals and unilateral amblyopes in under-two-year-olds. Indian journal of ophthalmology. 2003;51(4):341-5.

85. Sturm V, Cassel D, Eizenman M. Objective estimation of visual acuity with preferential looking. Investigative ophthalmology & visual science. 2011;52(2):708-13.

86. Mohan KM, Miller JM, Harvey EM, Gerhart KD, Apple HP, Apple D, et al. Assessment of Grating Acuity in Infants and Toddlers Using an Electronic Acuity Card: The Dobson Card. Journal of pediatric ophthalmology and strabismus. 2016;53(1):56-9.

87. Tailor V, Glaze S, Unwin H, Bowman R, Thompson G, Dahlmann-Noor A. Saccadic vector optokinetic perimetry in children with neurodisability or isolated visual pathway lesions: observational cohort study. The British journal of ophthalmology. 2016. **Figure 1**: The original forced-choice preferential looking apparatus with two cutouts for the stimuli. On the left is the grating pattern, and on the right is the luminance-matched blank.

Figure 2: Example of TACII card with a low spatial frequency square-wave grating on the left.