Preliminary Clinical Validation Of A New Picture–Based Visual Acuity Test In Children With Amblyopia: A Comparison Of The Auckland Optotypes (Tao) And Crowded Logmar Letters

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ABSTRACT

Background/aims

Amblyopia is the most common visual deficit in children and accurate visual acuity (VA) assessment is essential for diagnosis. While ETDRS high-contrast logMAR VA is the reference standard test for adults, less agreement exists for pre-literate children. A new picture optotype acuity test (The Auckland Optotypes; TAO) has shown favourable comparison to letter acuity charts but has not yet been evaluated in children with amblyopia. This study aimed to compare visual acuity (VA) obtained using TAO to crowded logMAR letters in children age 5-8 years with amblyopia.

Methods:

Children with amblyopia (n=54 [20.37% strabismic, 18.52% anisometropic, 61.11% mixed], mean age 78.30 ±11.72 months) were recruited from paediatric ophthalmology/orthoptic clinics at Moorfields Eye Hospital NHS Foundation Trust, London, and Cambridge Community Services NHS Trust, Bedford. Best corrected VA was measured in both the amblyopic eye (AE) and fellow eye (FE) using TAO and a crowded letter acuity chart. Bland-Altman analysis was used to measure 95% Limits of agreement (LoA) for VA measures captured (AE, FE and interocular difference [IOD]).

Results:

Good agreement between TAO and letter VA measurement was observed (mean bias: AE -0.01, FE 0.01, IOD -0.02). For AE measures 95% LoA were from -0.25 to 0.24 logMAR, this being similar for FE (-0.24 to 0.25) and IOD measures (-0.30 to 0.27).

Conclusion:

TAO and letters elicited similar VA in children with amblyopia. TAO could be a useful picture-based chart for paediatric vision assessment.

INTRODUCTION

Accurate measurement of visual acuity (VA) is central to the detection of amblyopia, the most common vision deficit in childhood, and the monitoring of treatment efficacy. Measuring VA in children is difficult and requires age-appropriate tests and experienced clinicians. The Early Treatment Diabetic Retinopathy Study (ETDRS) chart is the reference standard VA test for adults however, it is not suitable for pre-literate children. Picture-based vision charts have been designed to address this; however, these often have their own limitations, for example, overestimation of VA compared to letter optotypes (1-4). In the UK, in pre-literate children the Kay Picture test (1) is widely used. Clinical validation has shown that it overestimates visual acuity by 0.10-0.20 logMAR, compared to crowded letter tests (2, 3). In children with amblyopia, Kay Picture values have been found to differ from ETDRS measurements by around 0.20 logMAR. There has also been a suggestion of proportional bias, with increasing VA overestimate with worsening levels of VA (4). The Kay Pictures subsequently have been redesigned to address some of these issues but with limited validation (5).

Recently, a new picture optotype test, The Auckland Optotypes (TAO) has been developed (6). TAO are an open access set of psychometrically robust, picture optotypes. It consists of 10 optotypes which have a consistent stroke width, 1:1 aspect ratio and are fully enclosed with limited acute angles (figure 1). Existing evidence suggests that VA obtained with TAO is comparable to that obtained with ETDRS in adults. Similarly, strong agreement has been found between TAO and Sloan letters as well as Lea symbols in visually normal children (6-8). Such agreement is promising and suggests that TAO could enhance the accuracy of VA assessment in pre-literate children and potentially fulfil the criteria for a picture optotype test suitable for use in clinical trials. However, before TAO could be advocated for clinical or research use, validation in children with visual difficulties and in particular amblyopia is required.

The aim of this study was to examine the agreement of VA measurements obtained using TAO to that of the reference standard VA test for children with amblyopia –crowded logMAR letters (HOTV/Keeler Crowded logMAR).

METHODS

Participants

Fifty-four children aged 5-8 years (mean ±SD, 78.30 ±11.72 months) with unilateral amblyopia were recruited to this study between the 13th June 2019 – 27th February 2020. Amblyopia was defined as an interocular difference ≥0.20 logMAR, with fellow eye acuity of 0.20 logMAR or better. Children with a history of intraocular surgery, current ocular surface inflammation, glaucoma, cataract or developmental delay were excluded. Due to screen size limitations, participants with VA >1.40 logMAR were excluded. Ethical approval was obtained from the Research Ethics Committee London – Surrey (19/LO/0519). All procedures adhered to the tenets of the Declaration of Helsinki. Informed parental consent was obtained prior to study procedures and children also provided written assent where appropriate.

Psychophysical procedure

Study procedures were undertaken at Moorfields Eye Hospital NHS Foundation Trust, City Road, London (site 1) and Cambridgeshire Community NHS Trust, Bedford (site 2). At both sites, a consistent clinical testing room, was used for test presentation i.e., both optotype acuity tests were presented under the same room illumination and the test chart brightness was >80 cd/m^2 for all measures. Testing order of acuity tests was randomised using simple block randomisation.

At site 1, both TAO and letter (HOTV) tests were presented on a 19" GNR TS902 LCD monitor (pixel resolution 1280x1024, refresh rate 60Hz) via the COMPlog computerised system calibrated for a 3.5m viewing distance. The COMPlog testing algorithm employs an initial range finding phase whereby a single crowded optotype is presented in 0.20 logMAR steps until a single reversal is obtained. Threshold VA was then measured by presenting a single line of five optotypes, separated by half an optotype width and surrounded by an overall crowding box, decreasing in 0.10 logMAR intervals. If all five optotypes could not be simultaneously presented due to limitations in screen size, the lines were broken into smaller numbers of optotypes such that a cumulative total of five optotypes were presented for each line size. This was the case for both TAO and letter tests. The simultaneous presentation of five optotypes per line

could occur from 0.80 logMAR. Testing was terminated once all optotypes at a given VA level (i.e., a whole line) were incorrectly identified.

At site 2, TAO and letters were presented as hand-held tests at 3m distance. TAO was presented on a hand-held Microsoft Surface Go 10-inch tablet (screen resolution: 1800 x 1200, refresh rate: 60 Hz) via COMPlog, as above. Letter acuity was assessed using hand-held Keeler Crowded Acuity Cards in a similar two-stage process. Initially participants were asked to identify either the second or third letter on a line, decreasing in 0.20 logMAR steps until one letter was incorrectly identified. Threshold VA testing then began from the last correct response, decreasing in 0.10 logMAR intervals. Testing was terminated once all optotypes on the line were incorrectly identified.

Data collection was undertaken by experienced orthoptists/paediatric optometrist. An opaque occluder was used for uniocular testing; the amblyopic eye was always tested first. Participants were instructed to name the optotypes aloud; a matching card was permitted if required. A forced-choice procedure was employed in all cases to minimize the effect of observer criterion, i.e., if children were unsure of the optotype presented at threshold they were encouraged to attempt/guess before termination. Optotype presentation duration was unlimited and, in all cases, single optotype scoring was applied. VA was recorded in standard logMAR notation. A scaling factor (-0.216 logMAR) was applied to TAO measures to account for a different bounding box to stroke width ratio compared with Sloan letters (SC Dakin, personal communication, 2019). The stroke width / total optotype ratio for TAO is 1:8.23, compared to 1:5 for Snellen, 1:7 for Lea Symbols and 1:10 for Kay pictures. Therefore; such a scaling factor is required to achieve equivalence between different optotype sets (6).

Data Analysis

Analysis was conducted using MATLAB 2020a (The MathWorks Inc., USA). Bland-Altman Limits of Agreement (LoA) analysis was used to measure agreement between the VA tests. The upper and lower 95% LoA and associated 95% confidence intervals were calculated. Proportional bias was evaluated using Pearson's correlation and ordinary least squares linear regression analysis. VA measures in the amblyopic

eye (AE) and fellow eye (FE), in addition to interocular difference (IOD) were evaluated separately. Equality plots were also constructed for AE, FE and IOD comparisons between charts, with paired samples t-tests being undertaken to determine if there were statistically significant differences in these measures with each chart form. A three-way ANOVA with the fixed effects of chart type and testing site, together with the random effect of amblyopia severity was performed to examine what experimental factors may influence the IOD measures captured in this study. For the purposes of this analysis amblyopia severity was determined by logMAR letter acuity in the amblyopic eye. AE acuity <0.6 was considered moderate amblyopia and ≥0.6 severe amblyopia (9, 10). An α of 0.05 was considered statistically significant with holm-Bonferroni correction being applied to p-values where necessary.

RESULTS

All participants successfully completed both TAO and logMAR letter VA tests. Participant characteristics are detailed in Table 1.

Bland-Altman analysis indicated good agreement between TAO and crowded logMAR letters (Figure 2 a-c). LoA for FE measurements were ±0.25 logMAR, with similar values for AE (± 0.24 logMAR) and IOD (±0.32 logMAR). A paired t-test (with Holm-Bonferroni correction) also revealed there to be no statistically significant differences in either FE (P=0.49), AE (P=0.79) and IOD (P=0.45) measurements with either test examined. No statistically significant proportional bias between chart forms was observed for AE (r^2=0.04, p=0.16) and FE measures (r^2=0.06, p=0.07), but was evident for FE measures (r^2=0.08, p=0.04, fig. 2c) whereby IOD measures appeared to be underestimated by TAO relative to letter acuity measures when amblyopia was more dense. A similar trend may be observed from the equality plot examining the relationship between IOD measures with TAO and logMAR letter acuity (fig. 2e). Further examination also revealed there to be statistically significant interaction effects between study site and amblyopia grade ($F_{(1,107)}$=8, P=0.005) on IOD values. No other interaction effects were observed. Post-hoc analysis (fig. 3) revealed there be markedly lower IOD values in participants at site 2 compared to site 1(P<0.001, fig. 3c), this reflecting the fact relatively fewer patients with severe amblyopia were recruited at this site compared to site 1 (Table 1).

DISCUSSION

Good agreement was established between TAO and letter VA (Figure 2 a-c), indicating that TAO appears to be an equivalent measure to letter VA in children with amblyopia. The 95% LoA established in this study in the AE (±0.24 logMAR) and FE (±0.25 logMAR) were similar to, albeit slightly wider than, previously reported comparisons between TAO and logMAR letters in visually normal children (±0.20 logMAR) (7, 8). The LoA observed in this study are also in line with those for well-established and widely used picture acuity charts. For example, in a paediatric population the agreement between Lea Symbols and ETDRS has been shown to be in the region of 0.30 to -0.20 logMAR (11). While LoA between Kay Pictures and Keeler crowded logMAR charts, both of which have fewer optotype alternatives than TAO, has been reported as (0.225 to -0.030 logMAR) (3, 11, 12). However, TAO does appear advantageous as the mean bias observed in this analysis is lower than that reported for other picture acuity charts indicating closer agreement with VA measures with the reference standard ETDRS chart (3, 11, 12).

While there was no overall influence of study site on observed trends for IOD measures with each chart form (fig. 3a), site 1 did exhibit higher overall IOD values in children with severe amblyopia (AE ≥0.6 logMAR, fig. 3c). We hypothesise that this observed difference in overall IOD (across both chart forms) is a result of differences in the cohorts recruited at each study site, rather than any systematic differences between tests, investigators or study procedures at each site. Indeed, it may be seen from fig. 3c that a greater number of patients with dense amblyopia (as defined using logMAR letter VA) were recruited and tested at site 1 compared to site 2.

While we observed good agreement between TAO and letter VA, TAO appeared to underestimate IOD relative to letters in severe amblyopia (≥0.6 crowded letter logMAR, figures 2a, 3b). This underestimation is somewhat surprising as the agreement between amblyopic and fellow eye acuity using TAO compared to letter optotypes was a good level and similar LoA were found for either eye. We propose that this underestimation of IOD in severe amblyopia is a result of differences in TAO design compared to letters.

For example, TAO, consisting of 10 optotypes, contains more possible alternatives than the letters used in paediatric letter charts considered in this study. It has been demonstrated that the number of alternatives in a forced choice (AFC) test is inversely related to VA threshold measures (13, 14); the letter tests used in this study being truncated (COMPlog: 4-AFC, Keeler: 6-AFC) relative to TAO (10-AFC) which could contribute to lower IOD in severe amblyopia as there is increased probability of an incorrect "guess" at threshold with TAO. TAO optotypes also lack acute angles which could potentially increase their difficulty relative to letters at threshold (15, 16). Further examination of the equality plot comparing TAO and letter VA for the FE in the cohort examined (fig. 2e) would suggest that such issues appear to bias measures primarily at the higher VA range (better than 0.20 logMAR). It is also possible that this trend could also be attributed to the small participant sample within this VA range (n=14) or increased measurement variability in severe amblyopia. As this was an unexpected finding in this sample, further work with an appropriate sample size would be beneficial to specifically determine if IOD varies with amblyopia severity when examined with TAO and conventional tests. Further work incorporating inter and intra-test variability would also be useful to evaluate the precision of cross-sectional and longitudinal VA measures with TAO in amblyopia.

No proportional bias was observed with AE measures, this being evident in both the Bland-Altman (fig. 2a) and equality plots (fig.2d). This is particularly relevant in amblyopia as poorer AE VA triggers increased patching doses; thus, any VA overestimation could result in insufficient treatment for the severity of the condition. Therefore, TAO could be advantageous in the accurate estimate of AE acuity in pre-literate children.

CONCLUSIONS

This study describes the first comparison of TAO to logMAR letters in children with amblyopia. Good agreement was found between the tests, using a clinical testing protocol, suggesting that TAO could be appropriate for clinical VA measures in children with amblyopia. We recognise that this is a preliminary study and a larger sample size would be advantageous to expand on these findings. Further investigation of TAO VA measures in younger children and in severe amblyopia would be advantageous.

COMMERCIAL DISCLOSURES:

Mulholland PJ - Heidelberg Engineering & LKC Inc. (Research support)

Shah N - The Moorfields Acuity Chart (Co-inventor)

- COMPlog Clinical Vision Measurement Systems Ltd (Research support)

Dahlmann-Noor A – Santen Inc (Medical Advisor)

AUTHOR CONTRIBUTION STATEMENT:

SL was responsible for the initial study design and concept, protocol development, BIPOSA funding application, ethics application, recruitment of participants and drafting the final manuscript.

EMcV was responsible for the College of Optometrists funding application, assisting with ethics application, recruitment of participants and drafting the final manuscript.

NS was responsible for assisting in the College of Optometrists funding application and editing the final manuscript.

PJM was responsible for assisting in the College of Optometrists funding application and editing the final manuscript.

SM was responsible for the recruitment of participants at site 2.

ADN was responsible for the initial design and concept of the study, NIHR Biomedical Research Centre grant application, ethics application, overseeing the study and editing the final manuscript.

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CONFERENCE PRESENTATION: Presented in part at the British & Irish Paediatric Ophthalmology & Strabismus Association meeting 2019 (Edinburgh, UK).

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Gender – n	
Male	**28**
Female	**26**
Age (months) – Mean ±SD	**78.30 ±11.72**
Ethnicity – n	
White	**30**
Asian/British Asian	**10**
Black/Black British	**7**
Mixed	**4**
Other	**3**
Type of Amblyopia – n (%)	
Strabismic	**11 (20.37%)**
Anisometropic	**10 (18.52%)**
Mixed	**33 (61.11%)**
Refractive Error SE – Median (IQR)	
Amblyopic Eye	**4.32 (-0.19 to +6.75)**
Fellow Eye	**1.88 (+0.19 to +4.35)**

Table 1: Participant Characteristics. Where data is normally distributed mean ± standard deviation (SD) is reported. Where data was not normally distributed median (interquartile range) is reported.

FIGURES:

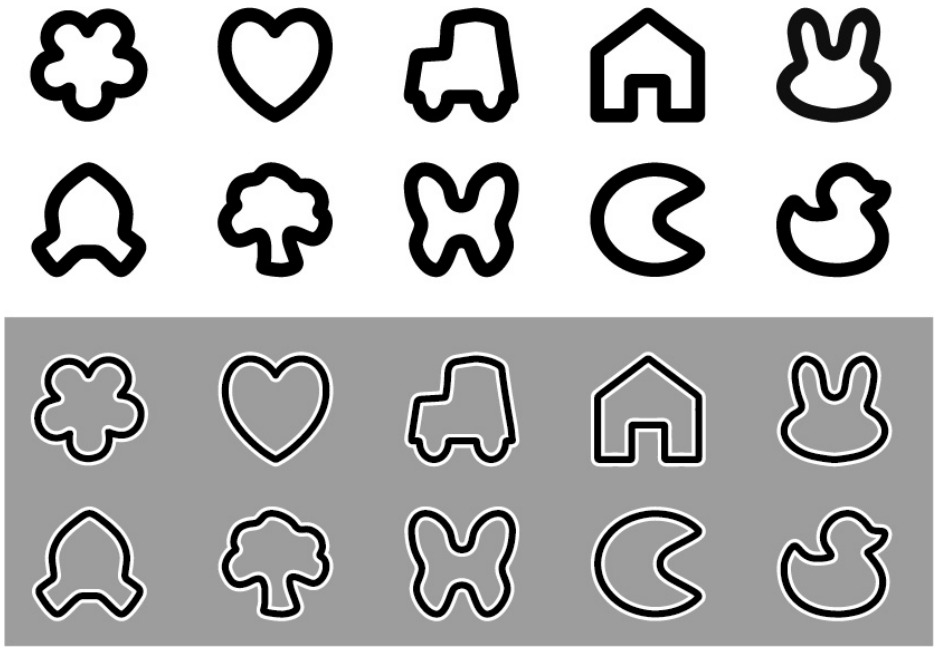

Figure 1. An illustration of The Auckland Optotypes in both regular and vanishing forms.

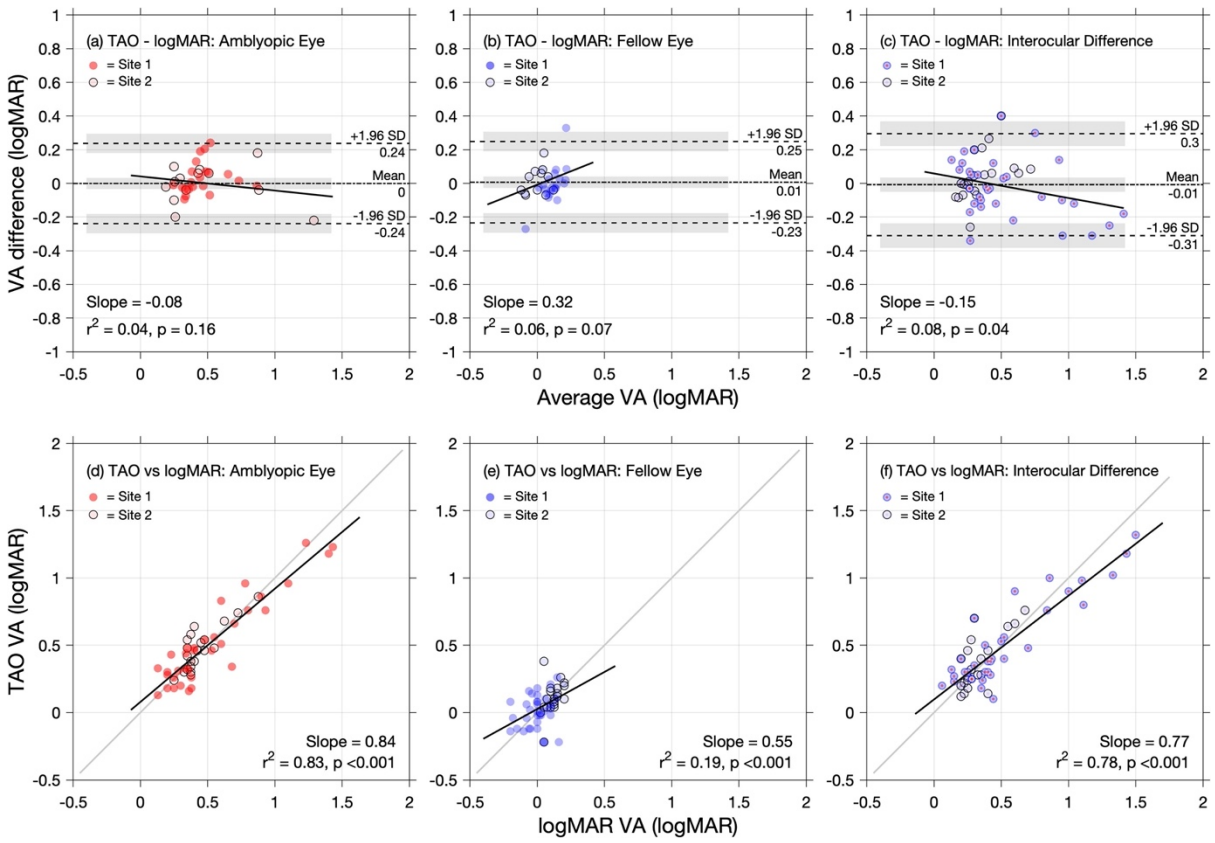

Figure 2. (a-c) Bland-Altman LoA plots indicate good agreement between TAO and crowded logMAR letters for the amblyopic eye (a), fellow eye (b) and interocular difference measures (c). 95% confidence intervals surrounding the 95% LOA are represented by grey shading with different plot markers for each test site. **(d-f)** Equality plots comparing TAO and logMAR. Ordinary least-squares linear regression line is included (black) along with an equality line (grey).

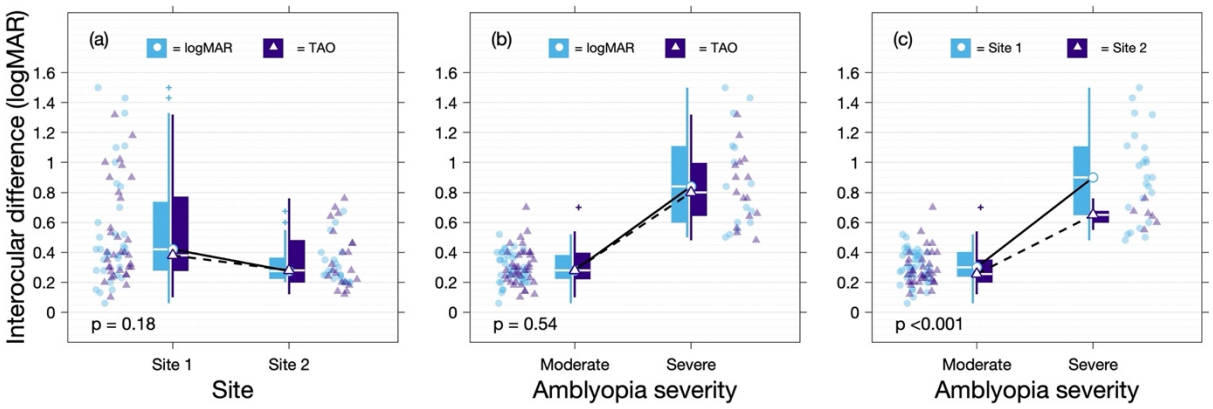

Figure 3. Interaction plots examining the effect of (a) experimental site and chart form, (b) logMAR letter VA level in the amblyopic eye (amblyopia severity) and chart form, and (c) logMAR letter VA level in the amblyopic eye (amblyopia severity) with test site on IOD values.