1. **Title Page.**

Visual acuity and contrast sensitivity with iPad. Comparison with Optec6500

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2. Structured abstract.

Purpose

To present two iPad applications (apps) for measuring Visual Acuity (VA) and Contrast Sensitivity Function (CSF) and to assess reliability and agreement with a commercial screening device.

Methods

Forty-five healthy subjects with monocular corrected visual acuities better than 0.2 logMAR participated in the agreement study of VA and CSF with iPad and Optec 6500. The measurement of VA was performed in accordance with the Amblyopia Treatment Study protocol with the AmblyopiaVA and the Early Treatment of Diabetic Retinopathy Study (ETDRS) with the Optec 6500. The CSF was measured with the ClinicCSF for iPad and the Functional Acuity Contrast Test (FACT) included in the Optec 6500. Twenty-five subjects from the total completed three sessions of measurements, one per week, and their results were considered in the test-retest study. We performed Bland-Altman analyses to assess the agreement and Deming regressions to calculate Mean Differences (MDs) and Limits of Agreement (LoAs). Coefficients of reproducibility (r) with exchangeable replicates were also computed.

Results

MD of VA was 0.06 logMAR better with AmblyopiaVA than with ETDRS ($p<0.001$) and LoAs were around ±0.2 logMAR. Test-retest reliability was better with AmblyopiaVA ($r=0.15$) with no statistically significant differences between days ($p>0.05$). A good agreement with no significant differences ($p>0.05$) was obtained with ClinicCSF and FACT. MDs were below 0.05 log units at all the spatial frequencies but non-constant LoAs were manifested at 3.6 and 18 cpd. Null hypotheses of same medians along days were accepted for both tests ($p>0.05$) but reliabilities were poorer with the increment of the spatial frequency.

Conclusions

The iPad tests showed a good agreement with conventional tests and may be a convenient and faster alternative to some existing commercial screening devices. On the other hand future improvements in test-retest reliabilities should be done for the screening of CSF.

Key Words: visual acuity, contrast sensitivity, screening, iPad

3. Main Text.

Introduction

Vision screening programs are intended to identify eye problems which occur in children[1] or adults[2] and refer them for further evaluation. Although there is a battery of screening methods designed to detect specific eye disorders, some screening techniques can be considered "multi-purpose," minimizing the need for several individual tests.[3] For instance, visual acuity (VA) is considered an essential part of any eye examination[4] and is used in the screening of refractive errors[5] and amblyopia.[6] On the other hand, Contrast Sensitivity Function (CSF) is considered an additional test for specialized clinical evaluation,[7] and has been generally accepted as a better predictor of visual performance than high contrast VA.[8,9,10]

Several tests and methods have been proposed for the assessment of VA and CSF. Nowadays, the Early Treatment of Diabetic Retinopathy Study (ETDRS) testing protocol is generally accepted as the gold standard of VA measurement in adults.[11,12,13] With regard to contrast sensitivity (CS), although the Pelli-Robson[14] chart is considered the gold standard to compare CS tests based on optotypes,[15] currently there is not a commercial gold standard test to measure CSF by sinusoidal gratings. An alternative could be to measure CSF using a computer-driven cathode ray tube (CRT), but CSF depends on several test parameters such as the psychophysical method, therefore differences may be found depending on the selected parameters.[16]

Despite the fact that commercial clinical tests are not able to measure absolute CSF like the CRTs methods do, they could be a good option to compare new screening tests since they are generally accepted by the research community.[17,18,19,20] Clinical CS tests commonly use 9 patches of sinusoidal gratings with different contrast levels. They could differ in the step sizes, ranges, or the psychophysical method to achieve the threshold.[19] The most used are the Functional Acuity Contrast Test (FACT)[21] and the Vector Vision CSV-1000.[22] Some devices which include VA and CS tests are available to screen vision such as the Optec 6500®,[23] which contains the ETDRS chart and the FACT test, and complies the ANSI standard.[24]

Ever since tablets appeared, new applications (apps) have been proposed in the field of visual science.[25,26,27] The big advantage of using these portable devices is the potential standardization of results since there are many common models which share characteristics such as screen chromaticity. Therefore, it can be hypothesized that if a developer takes into account the technical data of the tablets in the design of an app, any operator who uses the same device in any part of the world will approximately measure the visual function in the same conditions. However, it still has to be demonstrated that there are no changes in the screen properties among screens in the same tablet device.[28]

The assessment of the CS with a commercial tablet device (iPad) has recently been proposed under two different approaches: Dorr et al.[29] implemented the quick CSF method of Lesmes et al.[30] to evaluate 16 spatial frequencies log-spaced from 0.42 to 13.7 cycles per degree (cpd). This test was validated with measurements obtained from four normally sighted subjects on specialized laboratory equipment but it is rather time-consuming for screening purposes. On the other hand, Kollbaum et al.[27] developed a more elementary test consisting of two letters on each page of an iBook, having 0.1 log units of difference between pages. This test was compared to the Pelli-Robson and Freiburg Acuity and Contrast Tests and gave significantly lower values with the first one and good agreement with the second one. As a disadvantage, Kollbaum's test measures CS instead of CSF because it uses optotypes rather than sinusoidal gratings.

The aim of this study is to introduce two new iPad apps which represent an alternative to other expensive and large-format screening instruments, such as the *Optec6500*.[31] *AmblyopiaVA* and *ClinicCSF* are the names of these apps designed for a fast screening of VA and CSF, respectively. The VA and CS records and test-retest reliabilities are compared with those achieved with the *Optec6500* that contains the *ETDRS* and the *FACT*.[32]

Methods

The proposed apps were developed with ActionScript 3.0 programming language for mobile devices and then compiled for IOS with Adobe Flash Builder (Adobe Systems, Inc.). The tablet used to perform this research was an iPad third generation with retina

display (2048-by-1536-pixel resolution at 264 pixels per inch (ppi)). A Spyder4Elite colorimeter was used to measure the chromaticity of the iPad screen for maximum brightness and the room lighting was obtained with a LX1330B Luxmeter.

Visual Acuity (*AmblyopiaVA)*

In the *AmblyopiaVA* app, each subject had to recognize which of the four letters (HOTV) appeared isolated in the centre of the screen (Figure 1, left). On each visual acuity level, a black crowded optotype was presented over a white background with luminance of 342 cd/m^2. This value corresponded to the maximum brightness of the screen and was chosen to ensure that luminance was the same at all the trials. An automated psychophysical method described by the Amblyopia Treatment Study (ATS) testing protocol was used to reach the VA threshold,[33] thereby the operator needed only to push the corresponding button according to the answer given by the observer. An empty button was placed next to the HOTV buttons to be pressed when the observer could not recognize the letter. Even though the ATS protocol consists of a binocular pre-test and a monocular screening, the first one was omitted and subjects directly started with monocular screening at 0.8 logMAR. The reinforcement phase described in the ATS protocol was also omitted and the application automatically passed from phase 1 to phase 2. The presentation distance for the *AmblyopiaVA* app was 3 m and the time it took to complete each measurement was around one minute per eye.

Figure 1

Contrast Sensitivity (*ClinicCSF)*

In the *ClinicCSF* app, sinusoidal gratings were used as stimuli for spatial frequencies of 3, 6, 12 and 18 cpd. The contrast of gratings was determined by the luminance difference of the light and dark bars, as described by the Michelson contrast ratio.[34] The sinusoidal gratings appear in a vertical orientation or are tilted ±15º from the vertical and are masked by circular patches with blurred edges that fade the gratings into a grey background of mean luminance (85cd/m^2). The patch size was configured to subtend 1º of visual angle at a presentation distance of 2m. A total of 9 patches of different contrasts were generated for

each spatial frequency and each orientation. Stimuli were programmed with *MATLAB* software (The MathWorks, Natick, MA) and the library *COLORLAB*.[35] A more detailed description of the *ClinicCSF* design used in this study has recently been published as *ClinicCSFv2*.[36] The CS values for each level were the same as the FACT in order to obtain comparable results between instruments (Table 1). The psychophysical procedure was also programmed to follow the one used in the FACT. It consists of three steps: (1) starting at the first level, it goes up one level after each right answer until the observer fails; (2) the same procedure as the previous step but starting two levels below the level in which the answer was wrong in step 1; (3) the exam ends after two successive wrong responses, the CS threshold corresponding to the latest correct answer. The time it took to complete each measurement was around two minutes and a half per eye.

Table 1

Subjects and Procedures

Forty-five subjects, comprised of 21 males (mean age: 36 ± 11 years) and 24 females (mean age: 33 ± 10 years), were recruited from university staff and students at the University of Valencia. Exclusion criteria included strabismus or any cause of monocular reduced visual acuity worse than 0.2 logMAR with habitual correction (measured with *ETDRS*). Informed consent was obtained from each subject just before starting the procedures. The research was conducted in accordance with the principles laid down in the Declaration of Helsinki.

All trials were performed in the same room illumination (15 Lux). The same procedure was carried out in all sessions by the same operator and with the patient wearing the habitual correction. VA and CSF were measured with the iPad test and, after a short break, with the *Optec6500* using the *day testing* option (85cd/m^2 target illumination). Twenty-five subjects from the total were cited for two more sessions, spaced a week apart, in order to evaluate the reliability of both devices.

Statistical Analysis

Although both of the subjects' eyes were measured during testing procedures, only one was included in the agreement and reliability analyses after a random selection.[37] VA and CSF variables were not normally distributed therefore non-parametric tests were employed. Statistical significances of VA and CS inter-eyes and inter-test differences were assessed with the Wilcoxon signed-rank test. On the other hand, differences between tests followed an approximately normal distribution, therefore the Bland-Altman (BA) analysis was performed to evaluate the agreement between iPad apps and Optec6500 tests and to assess test-retest reliabilities.[38] The *MethComp (version 1.25)* package was used with the *R* statistics software *(version 3.1, R Development Core Team, 2014)* in order to complete the statistical analyses described below.

Agreement. Differences between measurements for each test were plotted against the average and the 95% limits of agreement (LoAs) were computed depending on whether the average difference and the variability of differences were constant throughout the range of measurement.[39] We checked the hypotheses of constant differences and constant standard deviations by means of a Deming regression (function *DA.reg*).[40] If the corresponding *p* values for both hypotheses were significant ($p<0.05$), conversion equations were employed on the plot and MDs or LoAs were represented considering linear correlations (function *BA.plot,* parameters *dif.type = "lin"*, *sd.type = "lin"*).

Reproducibility. A Friedman 2-way analysis of variance by ranks with multiple comparisons was used to evaluate differences in medians among the three days.[41] The residual standard deviation (σ_m) with each test was computed with the data from the subjects who completed a total of 3 sessions (replicates). LoAs were estimated again considering models of exchangeable or linked replicates. A random permutation (function *perm.repl*) was done comparing the resulted LoAs with the original data by a BA plot in order to apply the exchangeable or linked models proposed by Cartensen et al.[42] Since the random permutation of replicates had little effect in the LoAs, they were computed as exchangeable. LoAs of test differences were compared with the reproducibility coefficients

(*r*) of each test defined as $1.96 \times \sqrt{2} \times \sigma_m$ (exchangeable replicates) in order to know if test agreement might be related with test reliability (*RepCoef* in function *BA.est*).[42]

Results

Visual Acuity

No statistically significant differences were found in the comparison between right and left eyes with both tests, although as it can be seen in Figure 2A, the difference between eyes was higher with *ETDRS* (p=0.09) than with *AmblyopiaVA* (p=0.85) at around 0.1 logMAR. In the comparison between tests (Figure 2B), VA scores obtained with *AmblyopiaVA* had better results than those obtained with *ETDRS* with a MD of 0.06 logMAR (p<0.001). This difference would be approximately three letters on a logMAR chart with five letters per line. The null hypotheses of constant MDs and constant SDs were accepted (p>0.05) which suggest that *EDTRS* results could easily be predicted with the *AmblyopiaVA* along the range of visual acuities measured (-0.2 to 0.2) by simply subtracting MD from *AmblyopiaVA* results.

Figure 2

Friedman test showed significant median differences between days χ^2 (2, n=25) =12.15, p=0.002 with *ETDRS*. The median was 0 logMAR for the first day and -0.1 logMAR for the other two days. On the other hand, medians with *AmblyopiaVA* were -0.1 logMAR in the three days with no statistically significant differences among days χ^2 (2, n=25) =2.61, p=0.27. The number and percentage of subjects that reported differences within 0.1 logMAR in the three days were 24 (96%) with *AmblyopiaVA* and 21 (84%) with *ETDRS*. The permutation indicated that replicates should be treated as exchangeable, therefore a recalculation of LoAs was developed by this condition obtaining a value of ±0.2 logMAR, similar to that reported in the agreement study (Figure 2B). Coefficients of reliability (*r*) were 0.15 logMAR for *AmblyopiaVA* and 0.17 logMAR for *ETDRS*.

Contrast Sensitivity

The analyses of median differences between right and left eyes were not significant for all spatial frequencies and with both tests (p>0.05). There was a ceiling effect for spatial

frequencies of 3 and 6 cpd which was manifested by a negative skewed distribution in the box plot diagrams (Figure 3). Even though the distributions of *ClinicCSF* and *FACT* were less similar with the increment of the spatial frequency, no statistically significant differences were found at any spatial frequency ($p>0.05$).

Figure 3

MDs were below 0.05 log units for all spatial frequencies and LoAs were increased with the spatial frequency (Figure 4). Deming regression showed that although there were constant MDs for all the spatial frequencies ($p > 0.05$), constant SDs could not be assumed for 3, 6 and 18 cpd ($p < 0.05$). Therefore LoAs for non-constant SDs were also represented on BA plots with the corresponding equations to compute the LoAs along the average of test measurements (a).

Figure 4

Table 2 shows that even though no statistical significant differences were found in the Friedman analysis of variance of the three days, a low reproducibility was obtained with both tests and this was slightly better with the *FACT*. Considering step sizes between patches around 0.15 log units, reproducibility coefficients (r) from Table 2 correspond to a maximum difference of 2, 3, 4 and 4 patches for 3, 6, 12 and 18 cpd, respectively, with *ClinicCSF*. Reproducibility slightly improved to 2 patches for 3, 6, and 12 cpd while a maximum difference of 3 patches was obtained for 18 cpd with FACT. The r was very close to the LoAs, therefore the lack of agreement between *ClinicCSF* and *FACT* is mainly explained by the low reliability of both tests.

Table 2

Discussion

Visual Acuity

We found statistically significant differences between the records of VA obtained with *AmblyopiaVA* and *ETDRS*, resulting in a better VA of 0.06 logMAR with our test. This result is coincident with the outcomes reported by Rice M. et al.[43] who also found an MD of 0.06 logMAR between ATS and ETDRS. Leone J et al.[44] also found a better VA with the ATS procedure than with HOTV and ETDRS charts even though the latter ones incorporated a staircase method that improves the VA results.[13] Therefore, the apparent lack of agreement between tests in our study can be attributed to the differences in the VA protocols rather than to the use of different instruments (iPad Retina or Optec 6500). It is also important to note that even though non-statistically significant differences were found between eyes with both tests, lower differences were manifested with *AmblyopiaVA*, which might help in the amblyopia diagnosis with a lower rate of false positive referral rates.[44] In regards to test reliabilities, we obtained a better coefficient of reproducibility with *AmblyopiaVA* than with *ETDRS*. 96% of subjects reported differences within 0.1 logMAR with the *AmblyopiaVA*, this percentage is consistent with the 93% previously reported with ATS protocol.[33] This better reliability is mainly due to the ATS protocol. It is important to note that, even though we applied little modifications to reduce time testing (such as skipping the reinforcement phase), reliability has not been reduced. Therefore we believe that the reinforcement phase might not be necessary to improve testing reliability in the ATS procedure.

Unlike a previous work carried out with another VA test for iPad,[26] we did not have glare problems. Given that our study was conducted in a room without any kind of reflections over the screen, there is a possibility that dissimilar results would have arisen if the VA had been measured in a high light environment with reflections over the screen. One negative factor regarding our methodology might be that the brightness of the screen was set on the maximum level (342cd/m^2), which is over the recommended background luminance.[45] We decided to perform the study in this way to ensure that all evaluations were conducted under the same lighting conditions. Future work will concentrate on developing a system to measure environmental illumination and automatically set up the background luminance in accordance to the measured value.

Contrast Sensitivity

Dorr M. et al.[29] have recently demonstrated that CSF assessment on a mobile device may be indistinguishable from that obtained with specialized laboratory equipment. Although they implemented the quick CSF method[30] that reduces the testing time to no more than 5 minutes, this method could still be very time-consuming for screening procedures. Thus our proposal is a valuable alternative since it can be completed in half the time. The *ClinicCSF* results demonstrated a good agreement with *FACT* with no statistically significant differences between tests at any spatial frequency. Specifically, the MDs were lower than 0.05 log units for all spatial frequencies. In a previous work, Franco et al.[17] found MDs of 0.3, 0.08, 0.2 and 0.18 log units for 3, 6, 12 and 18 cpd respectively in the comparison between VCTS-6500 and CSV-1000. The differences were statistically significant probably because in that study they used tests which differ in step sizes between CS levels.

We found a lower agreement between tests at high spatial frequencies. It is important to note that this fact is related to test-retest reliabilities of *ClinicCSF* and *FACT* which were also poorer with the spatial frequency increment. Pesudovs et al.[19] also found similar test-retest reliabilities, being poorer with the increment of the spatial frequency even though this fact was not highlighted in their discussion. In addition, a non-constant standard deviation of test differences along the range of contrast sensitivities was manifested for spatial frequencies of 3, 6, and 18 cpd with wider LoAs with the decrease of CS. Although Kollbaum et. al[27] used optotypes which contain a wide range of spatial frequencies whose relative weight depend on the letter of its size unlike sinusoidal gratings,[46] they reported a reliability dependency with CS levels. Therefore, it is possible that the *ClinicCSF* and *FACT* reliabilities also vary in subjects who present any ocular disease that affects the CSF. *ClinicCSF* has several advantages in regards to the Kollbaum et. al test, including testing different spatial frequencies, random presentation of grating orientation to avoid the learning effect and the possibility of optimising the psychophysical method to improve reliability. Research into improving reliability with a better psychophysical method and adding depth to the performance of iPad screens to choose the most suitable contrast

patches are already in progress in our group. In fact, a staircase psychophysical procedure has recently demonstrated a considerable reduction of the LoAs.[36]

Both *ClinicCSF* and *FACT* presented ceiling effects for some spatial frequencies because of characteristics of the sample (healthy subjects wearing habitual correction). This suggests that subjects in the sample probably had a better CS than was achieved with both tests. This fact of screening CSF tests has been widely studied [47,48] and even though people with poor CS have not participated in our study it can be expected that a floor effect would be also presented with this other sample type.

Conclusion

In this work we have presented two iPad apps for screening visual performance by measuring VA and CS. These solutions are proposed as an alternative against expensive and large-format instruments, such as Optec6500, that are more difficult to transport and store than portable devices. Specifically, we have obtained very good results for the measurement of VA. Differences in VA measured with *AmblyopiaVA* and *ETDRS* can be attributed to the ATS procedure and are similar to those reported previously by other authors. In our case, the use of a standardized procedure improved test-retest reliability and thus we suggest that this app could be a valid low-cost alternative to the current electronic visual acuity system.[49] In addition, even though CS with *AmblyopiaVA* has not been assessed in this study, the app offers the possibility of measuring VA at different levels of contrast (0 to 100%). This is an interesting point for future clinical research considering current studies of perceptual learning in amblyopia cases.[50] This variation of CS added to fact that measurement of VA may be performed at multiple distances (40cm to 3m), makes *AmblyopiaVA* a test that can be used for other applications as a measurement of visual performance with multi-focal intraocular lenses or multi-focal contact lenses.

Regarding contrast sensitivity, we obtained similar results with *ClinicCSF* and *FACT*. In fact, the *ClinicCSF* has been developed with the same contrast sensitivity levels and testing procedure than the *FACT* to compare their results. Further developments are in progress to find the best contrast sensitivity levels for an iPad and to improve the reliability with another psychophysical method. Finally, it is important to note that the results of our study

correspond to normal subjects. Clinical studies are presently being conducted with *AmblyopiaVA* in amblyopic children and also with *ClinicCSF* in patients suffering from different ocular diseases.

Disclosure

Rodríguez-Vallejo, M. has designed and programmed the AmblyopiaVA and ClinicCSF apps which he currently distributes at the Apple Store with his own developer account. The other authors report no conflicts of interest and have no proprietary interest in any of the materials mentioned in this article.

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Figure Legends

Figure 1. iPad application patterns. Crowded optotype in the *AmblyopiaVA* (left) and sinusoidal grating in the *ClinicCSF* (right).

Figure 2. (A) Box plot diagrams showing visual acuities from right and left eyes measured with both visual acuity tests. (B) Bland–Altman plot showing the mean difference against the average of *AmblyopiaVA* and *ETDRS* (solid line), limits of agreement are also represented by dashed lines.

Figure 3. Box plot diagrams showing the contrast sensitivities obtained with ClinicCSF and FACT for spatial frequencies of 3, 6, 12 and 18 cpd. The boxes indicate the first and third quartiles, the dark horizontal lines represent the median, and the extreme horizontal lines are the minimum and maximum. Other points represent outliers.

Figure 4. Bland–Altman plots showing the mean difference against the average of ClinicCSF and FACT. Mean differences were nearly zero for all spatial frequencies even though the limits of agreement (dashed lines) were increased with the spatial frequency and with the decrease in average of contrast sensitivity for 3, 6 and 18 cpd. The variable *a* in the LoAs equations corresponds to the contrast sensitivity average from both tests.

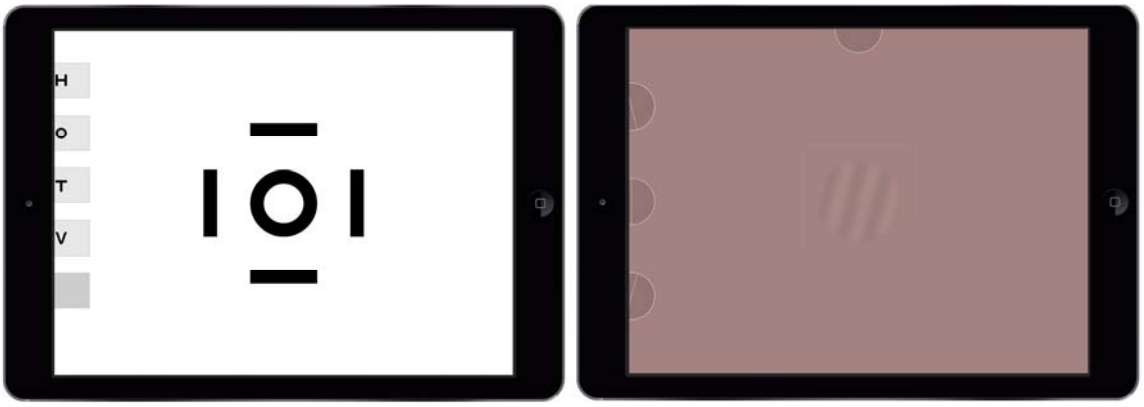

Figure 1

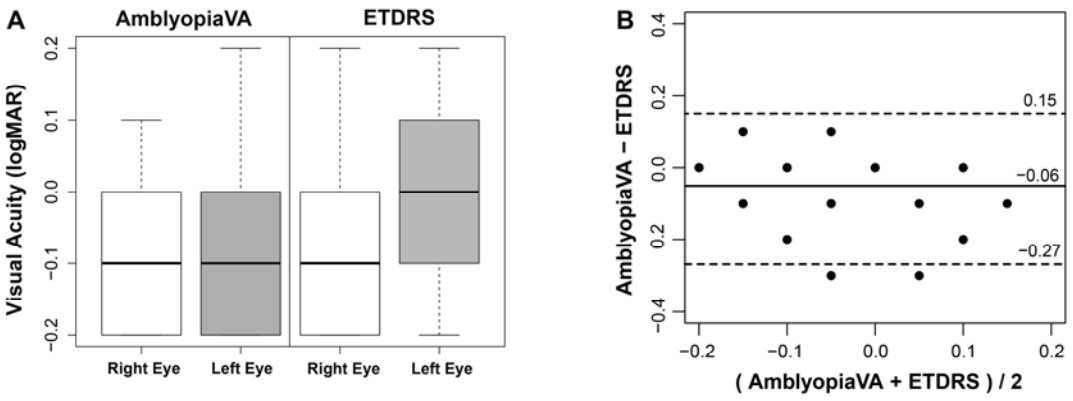
A
AmblyopiaVA
ETDRS
Visual Acuity (logMAR)
0.2
0.1
0.0
−0.1
−0.2
Right Eye
Left Eye
Right Eye
Left Eye
B
AmblyopiaVA − ETDRS
0.4
0.2
0.0
0.2
−0.4
0.15
−0.06
−0.27
−0.2
−0.1
0.0
0.1
0.2
(AmblyopiaVA + ETDRS) / 2

Figure 1

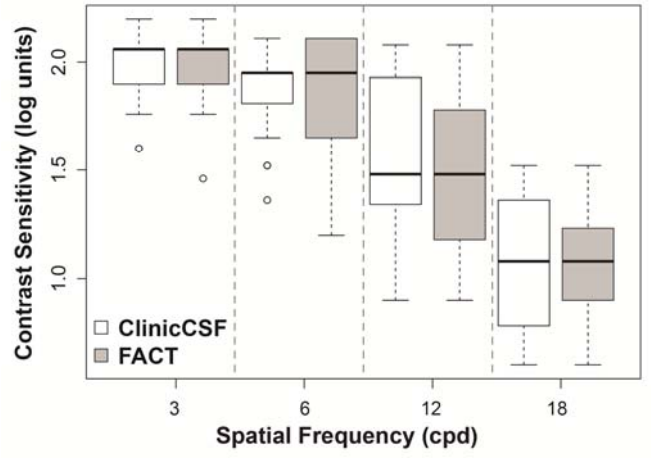
Contrast Sensitivity (log units)
1.0
1.5
2.0
ClinicCSF
FACT
3
6
12
18
Spatial Frequency (cpd)

Figure 3

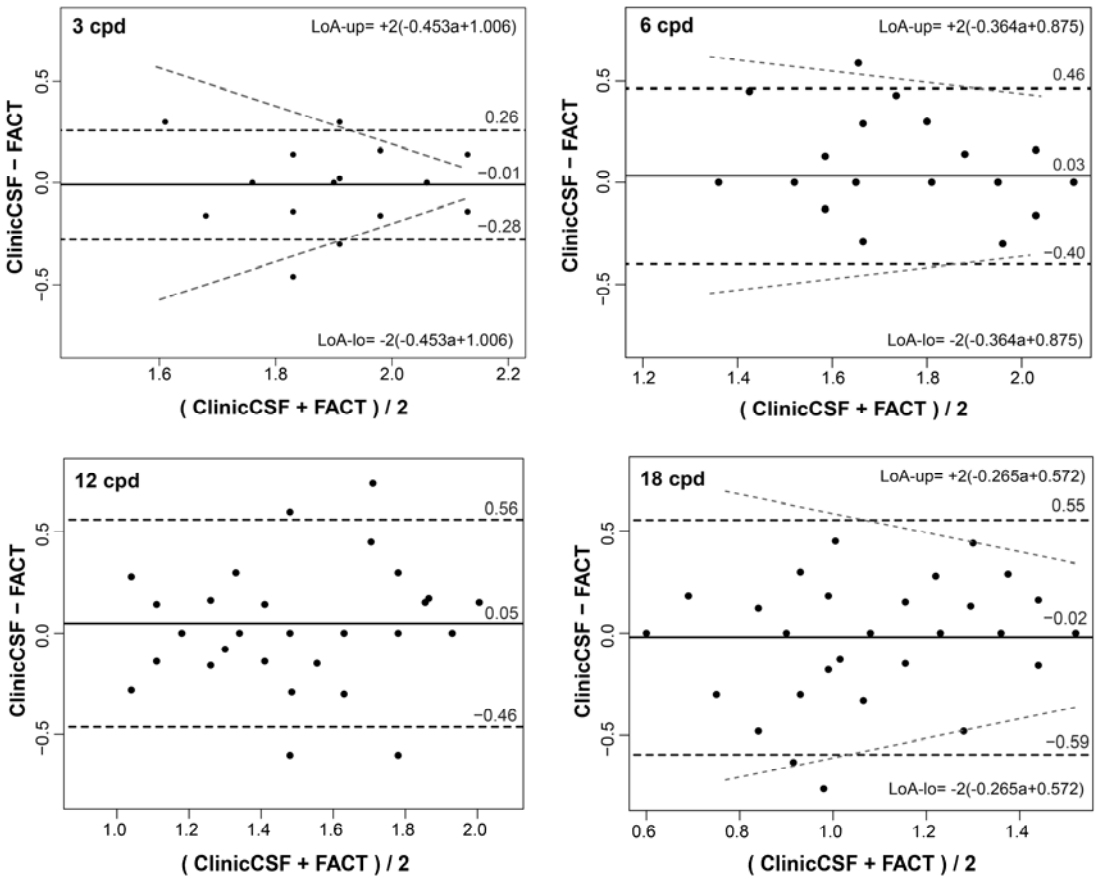
3 cpd
LoA-up= +2(-0.453a+1.006)
0.26
−0.01
−0.28
LoA-lo= -2(-0.453a+1.006)
ClinicCSF − FACT
(ClinicCSF + FACT) / 2
6 cpd
LoA-up= +2(-0.364a+0.875)
0.46
0.03
−0.40
LoA-lo= -2(-0.364a+0.875)
12 cpd
0.56
0.05
−0.46
18 cpd
LoA-up= +2(-0.265a+0.572)
0.55
−0.02
−0.59
LoA-lo= -2(-0.265a+0.572)

Figure 4