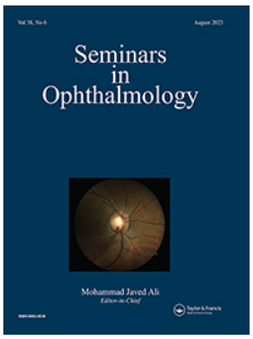

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Treatment of Anisometropic Amblyopia with a Dichoptic Digital Platform in Argentinian Children and Adults

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ABSTRACT

Purpose: To evaluate and compare the results of dichoptic training in Argentinian children and adults with anisometropic amblyopia.

Methods: Prospective non-comparative study enrolling 41 subjects with anisometropic amblyopia (age, 6–60 years old). Two groups were differentiated according to age, children (6–16 years, 24 subjects) and adults (>17 years, 17 subjects). All patients were treated with the Bynocs® platform (Kanohi Eye Pvt. Ltd, India) following a protocol of 30 sessions of training of 30 min daily 5 times a week for 6 weeks. Changes in corrected distance visual acuity (CDVA) and binocular function (BF) score with treatment were analyzed.

Results: In the whole sample, CDVA in the amblyopic eye improved significantly, with a mean change of 0.30 logMAR ($p < .001$). Likewise, a significant improvement was also found in BF score ($p < .001$), with a mean change of 1.14 log units. The change achieved in CDVA was significantly correlated with the baseline CDVA in the amblyopic eye (r=-0.568, $p < .001$). Furthermore, no significant differences were found between age groups in the change achieved in CDVA ($p = .431$) and BF with therapy ($p = .760$).

Conclusions: Dichoptic training with the digital platform evaluated provides an effective improvement of visual acuity and binocular function in children and adults with anisometropic amblyopia.

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KEYWORDS
Anisometropic amblyopia; binocular function; dichoptic training; stereopsis; visual acuity

INTRODUCTION

Dichoptic stimulation has shown to be an efficacious and safe treatment option of anisometropic amblyopia after a previous appropriate refractive correction.[1–13] This therapeutic option provides a simultaneous and separate stimulation of both eyes to eliminate the interocular suppression which has a primary role in the development of amblyopia.[14] The interruption or weakening of binocular vision during childhood due to a factor such as anisometropia can promote different levels of interocular suppression which are associated to different levels of visual acuity reduction.[15] Considering this, different dichoptic platforms have been developed and commercially released to treat amblyopia, being most of them investigated in a great variety of studies.[1–13] Differences between studies in terms of visual recovery can be due to several factors, such as the type of population selected or the clinical protocols followed, but also to the type of stimuli and the psychophysical method used which can be critical for an enhanced treatment effect. For this reason, any new platform or system for the treatment of anisometropic amblyopia has to be tested and investigated in detail despite using a dichoptic environment as other factors can contribute or not to a more optimized outcome.

One of the digital systems that is currently available for amblyopia treatment is Bynocs (Kanohi Eye Pvt. Ltd, India), which is an online platform including a variety of games based on dichoptic stimulation and using different environments, allowing children to play while an effective stimulation is performed.[5] A previous retrospective study to evaluate this platform in 161 Indian children with anisometropic or isometropic amblyopia was performed by Abdal et al.,[5] reporting a mean visual improvement in the non-dominant eye of 0.39 logMAR (almost 4 lines), with an associated improvement of the binocular function. The aim of the current study was to evaluate prospectively the results of this visual training technology in a sample of Argentinian children and also adults with anisometropic amblyopia, confirming if the results obtained are comparable to those previously reported with the same platform and even to those obtained with other systems.

METHODS

Patients

This was a prospective non-comparative study enrolling 41 subjects with anisometropic amblyopia and ages ranging from 6 to 60 years old that attended to the Department of Ophthalmology of the Regional Hospital Luis Pasteur Villa María in Cordoba (Argentina). Before their inclusion in the study, all of them were informed about the nature of the study and signed an informed consent following the tenets of the Declaration of Helsinki. Likewise, the protocol was approved by the Ethics Committee of the Hospital.

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Inclusion criteria for the study were as follows: age of 6 years old or more, moderate (visual acuity in non-dominant eye from 0.7 to 0.3 LogMAR) to mild (>0.3) amblyopia, previous prescription of the most adequate refractive correction (8 weeks at least), access to internet connection at home and use of an 11-inch monitor computer with an external keyboard. Exclusion criteria were as follows: children younger than 6 years old, presence of strabismus except in case of intermittent strabismus with binocularity, active ocular pathology, previous ocular surgeries, previous retinal diseases and any amblyopia treatment such as patching, atropine penalisation, Bangerter filter, or vision therapy done in past 2 weeks.

Clinical Protocol

All patients underwent a comprehensive eye examination including anamnesis, manifest and cycloplegic refraction, measurement of corrected distance visual acuity (CDVA) with a LogMAR chart, 4-dot Worth test, fixation analysis by visuscopy, stereoacuity (Bynocs platform), evaluation of the ocular alignment with the cover test, anterior segment evaluation with slit lamp and fundus evaluation under dilation. At the end of the training program, CDVA and stereoacuity were tested again under the same conditions to check the improvement achieved.

The Bynocs® platform was used for the vision therapy, activating the Amblyopia therapy protocol that consisted of 30 sessions of training of 30 min daily 5 times a week for 6 weeks. In each session, different games could be recommended. In the first 10 sessions, dichoptic exercises were prescribed, consisting of scenes (SuperCar, SuperMan) that were mostly seen by the dominant eye (use of red-blue goggles for dissociation), while one crucial stimulus for the performance of the game was only seen by the non-dominant eye. Once finished this part of the therapy, stereopsis (SuperBee) and fusional vergence exercises were included in the daily protocol of training. The size of stimuli and the duration of each exercise (maintaining a total training time of 30 min) could be modified according to the level of progression of the patient.

Statistical Analysis

The statistical data analysis was performed using the software SPSS version 25.0 for Windows (IBM Corp., Armonk, NY, USA). For the analysis of the level of binocularity, the binocular function score (BF) was calculated, considering the following: value of 5 as suppression, value of 4 as simultaneous vision or flat fusion and from 1.6 to 3.3 (log 40 arc sec log 2000 arc sec) the presence of stereopsis.[16]The Kolmogorov–Smirnov normality test was performed, and CDVA and BF data were found to be not normally distributed. Nonparametric statistical tests were then applied for the data analysis. Specifically, the Wilcoxon test was used to analyse the significance of differences in CDVA and BF before and after the visual training, whereas the Mann–Whitney test was used to analyse the differences between children and adult groups. The Spearman correlation coefficient was calculated to evaluate the level of correlation between the visual change achieved and different baseline conditions.

RESULTS

A total of 41 participants, with ages ranging from 6 to 60 years old (mean: 20.5; standard deviation (SD): 13.4; median: 14.0 years) were examined and treated in the current study. Two groups were created according to age: children, with ages ranging from 6 to 16 (24 subjects, 58.5%), and adults, with ages of 17 years old or more (17 subjects, 41.5%). The distribution of the sample in terms of gender was as follows: 22 males (53.7%) and 19 females (46.3%). Mean sphere was 1.05 D (SD: 2.56; median: 0.50; range: −5,50 to 6,75 D) and 1.94 D (SD: 4.03; median: 2.75; range: −8.00 to 7.75 D) in the dominant and amblyopic eyes, respectively ($p = .009$). Concerning cylinder, its mean value was −0.67 D (SD: 0.97; median: 0.00; range: −3.75 to 0.00 D) and −1.71 D (SD: 1.53; median: −1.25; range: −6.00 to 0.00 D) in the dominant and amblyopic eyes, respectively ($p < .001$).

Analysis of the Whole Sample

In the whole sample, CDVA in the amblyopic eye improved significantly with the training, with a mean change of 0.30 logMAR (3 logMAR lines) ($p < .001$). At baseline, any patient reached a CDVA of 0.10 logMAR or better, whereas after the training a total of 65.8% of subjects had this level of CDVA. Likewise, a significant improvement was also found in BF score ($p < .001$), with a mean change of 1.14 log units with therapy. Figure 1 shows the change in the distribution of measurements of near stereopsis with therapy. As shown, no measurable stereopsis was present in 43.9% of subjects before therapy, whereas this percentage decreased to 0.0% after the training. The change achieved in CDVA was significantly correlated with the baseline CDVA in the amblyopic eye ($r = −0.568$, $p < .001$) (Figure 2). However, no significant correlation was found between the change in CDVA achieved with therapy and age ($r = 0.260$, $p = .101$).

Comparative Analysis Children Vs. Adults

Table 1 summarizes the outcomes obtained in the group of children and adults of the sample. As shown, no significant differences in visual acuity, BF score and refraction were found among age groups at baseline ($p \geq .062$). Likewise, no significant differences were found either among groups after therapy in CDVA ($p = .670$) and BF score ($p = .364$). Consequently, no significant differences were found between groups in the change achieved in CDVA (Figure 3) ($p = .431$) and BF with therapy (Figure 4) ($p = .760$). Specifically, BF after therapy was between 3.3 (stereoacuity 2000") and 1.0 (stereoacuity 10") log units in all cases in both children and adult groups (Figure 5). Age was not significantly correlated with changes in CDVA (children: $r = 0.200$, $p = .349$; adults: $r = 0.377$, $p = .136$) and BF after therapy in any of the two groups evaluated.

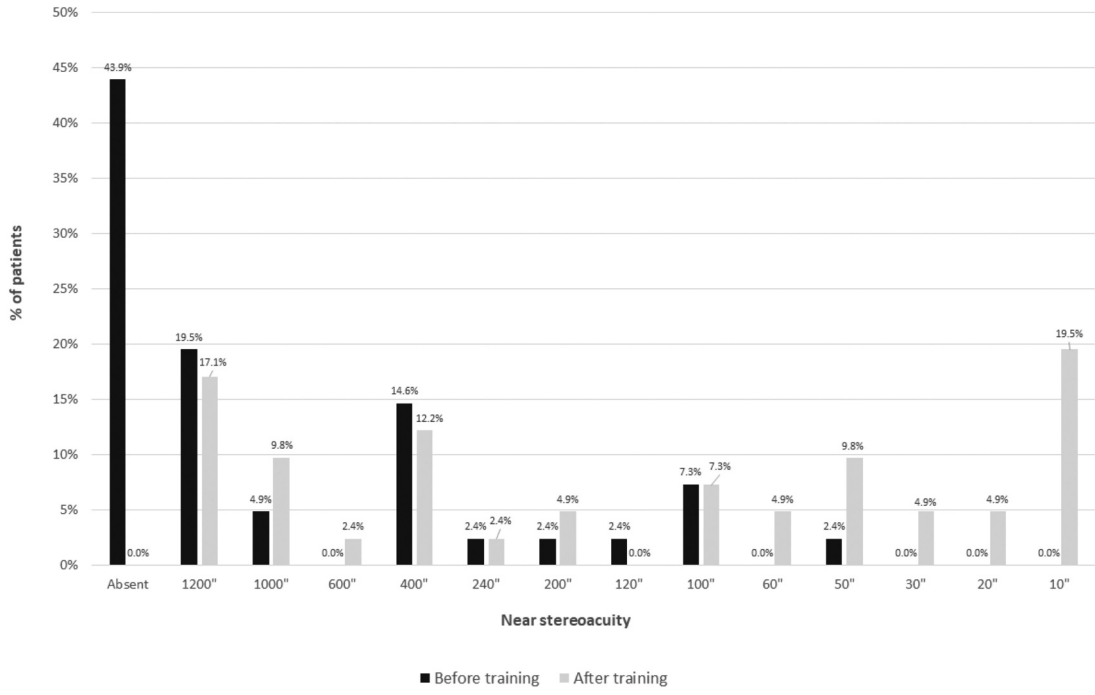

Figure 1. Distribution of near stereoacuity before and after visual training in the whole sample evaluated.

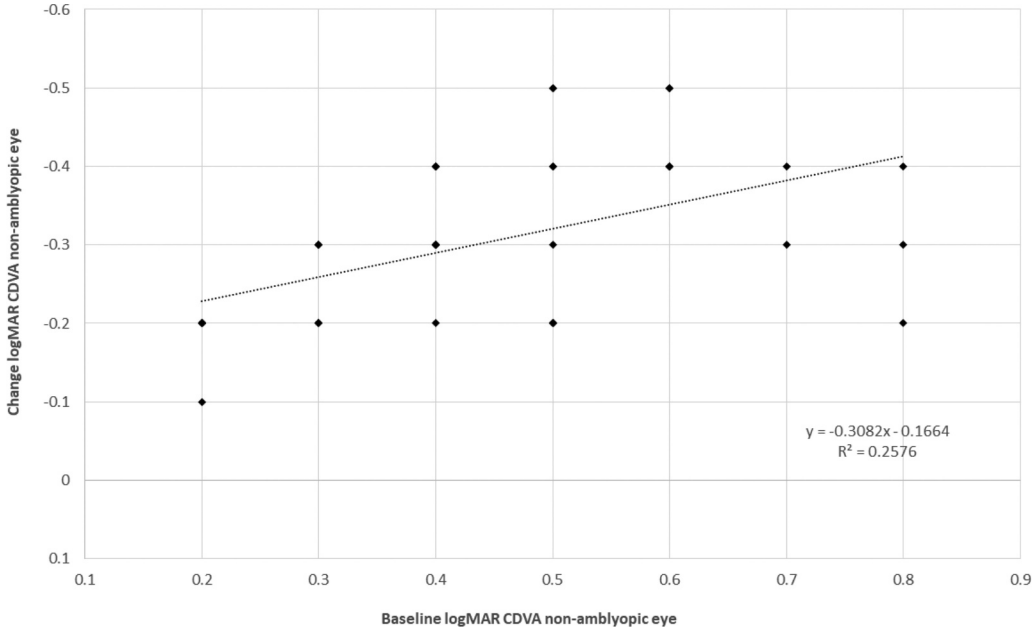

Figure 2. Scatter plot showing the relationship between the change in corrected distance visual acuity (CDVA) in the non-amblyopic eye and the baseline CDVA in such eye. The adjusting line to the data obtained by means of the least-squares fit is shown.

DISCUSSION

This study investigates the effect of visual training using the dichoptic therapy technology Bynocs in anisometropic amblyopia. Although there is some previous evidence of the efficacy of this technology in amblyopic children, the current study is the first to this date evaluating the effect in adults and compare it with that obtained in children. Specifically, in the current study, a significant improvement of visual acuity and binocular function has been obtained after a 6-week dichoptic training using a specific digital platform, Bynocs, in a sample of anisometropic amblyopes. Specifically, a mean improvement of 3 logMAR lines of CDVA was found in the series analysed as well as a mean improvement of BF score of 1.14 log units. This is consistent with the results from a large variety of studies evaluating the effect of dichoptic training in anisometropic amblyopia using different training systems.[1–13] Among them, Abdal et al.[5] investigated the efficacy of the same digital platform used in the current series in a large sample of isometropic and anisometropic amblyopes. These authors found somewhat better outcomes, with a mean change with therapy

Table 1. Summary of the main outcomes obtained in children and adult groups.

Mean (SD) Median (Range)	Children	Adult	p-value
Age (years)	11.0 (2.7) 10.0 (8.0 to 16.0)	34.0 (12.0) 32.0 (18.0 to 56.0)	<.001
Sphere (D)	1.59 (2.90)	0.28 (1.80)	.073
Dominant eye	1.00 (−5.50 to 6.75)	0.00 (−2.75 to 5.25)	
Cylinder (D)	−0.75 (0.98)	−0.56 (0.99)	.261
Dominant eye	−0.38 (−3.75 to 0.00)	0.00 (−2.75 to 0.00)	
Sphere (D)	2.79 (4.04)	0.74 (3.82)	.062
Amblyopic eye	3.75 (−7.00 to 7.75)	0.50 (−8.00 to 6.00)	
Cylinder (D)	−1.68 (1.21)	−1.77 (1.94)	.559
Amblyopic eye	−1.38 (−5.00 to 0.00)	−1.25 (−6.00 to 0.00)	
Pre-therapy logMAR	0.46 (0.16)	0.42 (0.20)	.468
CDVA amblyopic eye	0.40 (0.20 to 0.80)	0.40 (0.20 to 0.80)	
Post-therapy logMAR	0.15 (0.16)	0.13 (0.15)	.670
CDVA amblyopic eye	0.10 (0.00 to 0.60)	0.10 (0.00 to 0.50)	
Pre-therapy BF	3.32 (0.72)	3.13 (0.82)	.420
amblyopic eye	3.08 (1.70 to 4.00)	3.08 (2.00 to 4.00)	
Pre-therapy BF	2.20 (0.78)	1.97 (0.79)	.364
amblyopic eye	2.45 (1.00 to 3.08)	1.78 (1.00 to 3.08)	

*Abbreviations: D, diopter; CDVA, corrected distance visual acuity; BF, binocular function.

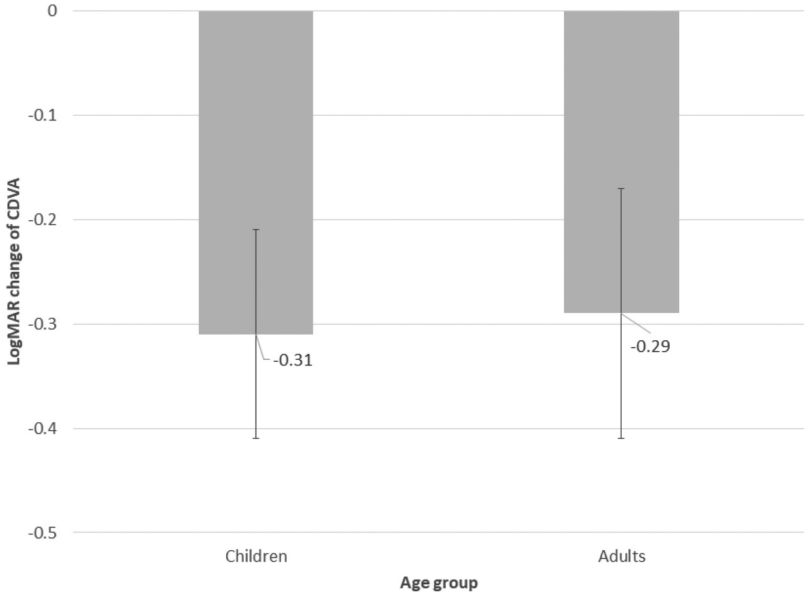

Figure 3. Mean change in logMAR corrected distance visual acuity (CDVA) after therapy in children and adult groups of the sample evaluated.

in CDVA and BF of 0.39 logMAR (almost 4 logMAR lines) and 1.55 log units, respectively.[5] It should be considered that the sample treated by these authors only included children, with a large proportion of cases of severe amblyopia compared to our series that have more potential range of improvement. Indeed, Abdal et al.[5] found a correlation between the change achieved in CDVA and the baseline level of CDVA ($r = -0.584$, $p < .001$), with more visual improvement in those eyes with worse baseline visual acuity. In the current series, a very similar level of correlation was found between the change in CDVA after the visual training program and baseline CDVA ($r = -0.568$, $p < .001$), confirming a great level of agreement of the outcomes among studies. It should be considered that a very similar clinical protocol was followed in both studies.

When analysing the changes reported by other authors with other dichoptic training platforms, care should be taken as there are quite relevant differences between studies in the clinical protocols followed, the methods used to measure the visual acuity and stereopsis, the type of stimuli used in the dichoptic dissociation during therapy, level of compliance and the duration of the training program. Huang and colleagues[4] found a mean improvement of CDVA of 0.32 logMAR with dichoptic training in a sample of amblyopic children from 7 to 10 years old no longer responsive to occlusion therapy, but these authors combined cases of anisometropic and strabismic amblyopia. In the same line, Bossi et al.[13] reported a mean improvement of CDVA with dichoptic training of 0.27 logMAR in children (age, 3–11 years) with anisometropic, strabismic or mixed amblyopia, with good level of compliance with treatment associated (89.4 ± 24.2%). Recently, Wygnanski-Jaffe et al.[1] confirmed that binocular vision training in anisometropic, small angle strabismic or mixed amblyopic children (4 to <9 years old) provided a visual improvement that was not inferior to patching (0.28 ± 0.13 vs. 0.23 ± 0.14 logMAR), with higher levels of adherence to treatment (91% vs. 83%, $p = .011$).

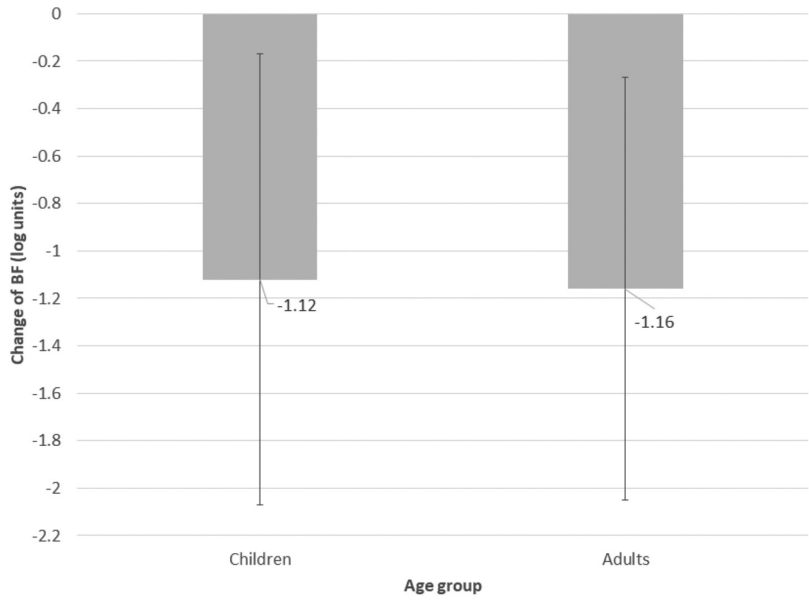

Figure 4. Mean change in binocular function (BF) score after therapy in children and adult groups of the sample evaluated.

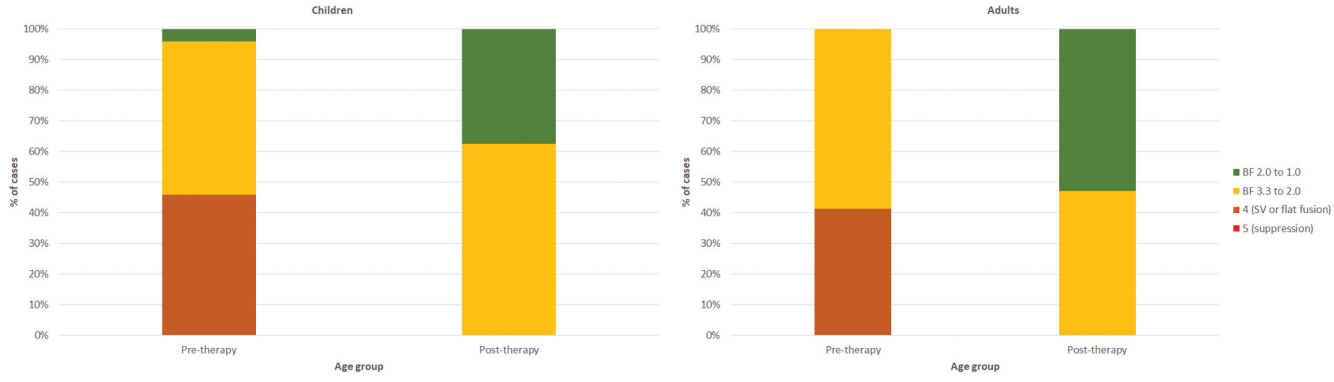

Figure 5. Distribution of preoperative and postoperative binocular function (BF) score in both children and adult groups before and after therapy.

For the analysis of the impact on binocularity of the dichoptic training used, a composite score, BF, was used that allows analysing the effect of the therapy on binocular vision not only considering those cases in which stereopsis was measurable but also cases presenting suppression or simultaneous vision without measurable stereopsis.[16] In our sample, BF decreased significantly which was associated to a significant improvement in stereoacuity, with any case presenting suppression after therapy. This is consistent with the result of some previous experiences evaluating the impact of dichoptic training on stereopsis.[1,2,4,9,12] Wygnanski-Jaffe et al.[1] reported a stereoacuity improvement of 0.40 log arcseconds after binocular training in a large sample of children 4 to <9 years with anisometropic, small-angle strabismic or mixed-mechanism amblyopia. Huang et al.[4] reported a significant change of stereoacuity after 3 months of dichoptic training in amblyopic children of 7–10 years old (from 190.00 ± 163.34 to 85.00 ± 61.24 arc sec). It should be considered that previous studies not using BF have only analysed the effect of therapy in those patients with measurable stereopsis, without the possibility of quantifying changes occurring in patients with suppression or not measurable stereopsis at baseline.

One differential aspect of this study compared to most of previous experiences is the combination of children and adults in the same sample. In any case, this is not the first experience reporting the efficacy of dichoptic training in adult anisometropic amblyopia, with several previous case series confirming this finding.[17,18–26] However, to our knowledge, there are no previous experiences comparing the visual improvement achieved after dichoptic training in children and adults. In our series, no significant differences were found between children and adult groups in the visual and binocular function improvements achieved with therapy, suggesting a similarity in the potential range of improvement in anisometropic amblyopia in children and adults. Indeed, no significant correlation of age with the change in logMAR CDVA induced with the treatment was found. It should be considered that no significant differences were found at baseline between adults and children in our series and therefore both amblyopic groups had similar distribution in terms of the severity of the condition.

The similar response between adults and children with the dichoptic training tested might seem contradictory as the level of plasticity is not the same. However, it should

be considered that an active training was used which adapted progressively the level of difficulty according to the level of improvement obtained in each session. The visual acuity and binocular improvements were achieved in children due to the elimination of the interocular suppression that has been shown to play a key role in the visual deficits associated with anisometropic amblyopia.[27] This interocular suppression has a common suppression mechanism at the early stage in the pathway, but with some potential additional extra-striate contributions affecting both dorsal and ventral streams differentially.[28] However, the mechanisms of recovery of visual function in adult anisometropic amblyopia seems to be more complex and not only due to the elimination of interocular suppression. [29,30] Liu and Zhang[30] suggested that dichoptic training may strengthen top-down attention to amblyopic eyes to counter the impacts of attentional bias to fellow eyes and/or physiological interocular suppression, promoting the improvement in stereoacuity. More research is still needed to better understand the differential aspects between the mechanisms of visual recovery with dichoptic training in children and adult patients with anisometropic amblyopia.

Finally, the limitations of the current study should be acknowledged. The main limitation is the sample size that was limited, especially when subdividing the sample into children and adult groups. However, despite this limitation, significant changes were detected that were also consistent with the outcomes of previous studies. An additional limitation could be considered the lack of control study or placebo group, but it should be considered that the aim of the current study was not to confirm the superiority of dichoptic training over other therapeutic options. It should be considered that there are some previous trials comparing dichoptic therapy with other options of treatment, such as occlusion.[1–4,6]

In conclusion, dichoptic training with the digital platform Bynocs provides an effective improvement of visual acuity and binocular function in children and adults with anisometropic amblyopia. A greater potential visual improvement with this therapeutic option is expected in those eyes with lower levels of visual acuity at baseline. More studies are needed to investigate the effect of this type of training in strabismic or mixed amblyopia. Likewise, this study was conducted in a sample of Argentinian children and adults, and the results obtained should be considered with care and confirmed in other samples including people from different ethnic groups to confirm if the effect of amblyopia treatment is affected or not by ethnicity. To this date, the efficacy of this option of treatment has been also confirmed in a pediatric population from India.[5]

Disclosure statement

No potential conflict of interest was reported by the author(s).

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