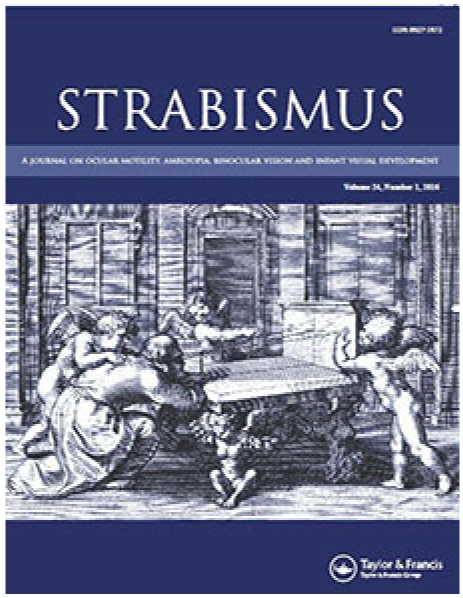

Visual-acuity increase in meridional amblyopia by exercises with moving gratings a compared to stationary gratings

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Visual-acuity increase in meridional amblyopia by exercises with moving gratings a compared to stationary gratings

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Meridional amblyopia, e-health, functionally assisted visual occlusion

Abstract

Background: The aim of the present work was to investigate the effect of a novel therapy, termed Focal Ambient Visual Acuity Stimulation (FAVAS), on the visual acuity development in patients with meridional amblyopia. We compared FAVAS containing moving vs. stationary gratings (sham FAVAS) as a combination therapy in patients treated with occlusion.

Methods: Patients were randomly allocated in two groups which all received a standard occlusion regimen. The first group consisted of 17 children (34 eyes) aged 10 to 13 (average 11.6 ± 0.3) years. The second group consisted of 20 children (40 eyes) aged 9 to 14 (average 12.5 ±0.4) years. In combination with occlusion, using a cross-over design, the first group was alternately exercised 10 days with a moving (FAVAS) followed by 10 days with a stationary grating stimulus (sham FAVAS), and the second group vice versa. The main objective is to investigate the treatment-dependent meridional training effects on the best corrected visual acuity in both groups.

Results: For both groups, the visual acuity was significantly increased only in the training stage with a series of exercises with the moving sinusoidal grating (FAVAS). Thereby the visual acuity along different meridians, showed such a statistically significant improvement induced by the moving grating coincident with alignment of the directional optical characters close to the meridian with maximal ametropia. No significant improvement was induced by the moving grating in the perpendicular thereto orientation with minimal ametropia. After the training stage using the stationary grating (sham FAVAS), however, there was found no statistically significant improvement, regardless of meridian.

Conclusions: Visual training of patients with meridional amblyopia by a series of online exercises using special computer games which contained moving gratings as a background stimulus (FAVAS) resulted in a statistically significant improvement of visual acuity development. At the same time, no statistically significant improvement was achieved after the respective analogue exercise series of the control condition with stationary gratings (sham FAVAS).

The most significant improvements were found in the meridian with maximum ametropia. Significantly less effects were found in the meridian with minimum ametropia.

Introduction

Amblyopia is one of the most common ophthalmological disorders in young patients with a prevalence of 5-6 % [13]. While affected children are impacted in their daily activities and future job selection, it also increases the risk of a severe trauma for the better eye [34]. Since Sattler [46] re-introduced into the practice of applied strabology the method of occlusion, i.e. the patching of the fellow sound eye, it was indisputably accepted as the gold standard of modern amblyopia therapy. Starting the occlusion early and adhering to it persistently, are two important factors that influence the effectiveness of this treatment. It has been shown that delayed diagnosis and treatment results in poor outcome [6].

On the other hand, notwithstanding that therapeutic strategies such as patching have been established in clinical practice for a long time, their success has been limited with a high rate of patients being resistant to therapy or not reaching normal visual acuity [3]. In view of this, pleoptics, as a system of visual exercises and stimulation methods in support of the standard occlusion procedure, had been developed early as a complementary treatment of amblyopia [4, 9, 12, 39, 40]. Although the concept of pleoptics is well known and established for many decades, this approach was not only complicated, time-consuming, but also requiring well-trained specialists; in sum, pleoptics requires an insupportably high expenditure of face-to-face therapy hours for patients and medical staff.

Recently, a paradigm shift in the therapeutic approach is aiming not at merely occluding the better eye, but rather additionally stimulating the amblyopic eye in line with pleoptic tradition. This is achieved with the aid of computer games, behind which there is a therapeutic stimulation concept and which thus make it possible that patients carry out pleoptic training online at home in combination with occlusion. Notably, a therapeutic software-based visual stimulation system for the complementary treatment of amblyopia had been developed two decades ago [23, 24, 25, 32, 37] by an interdisciplinary team of the Dresden University's ophthalmologic clinics (Theo Seiler), the department of psychology (Uwe Kämpf), the faculty of informatics (Wilfried Mascolus) and including scientific partners (UKE Hamburg, Wolfgang Haase). It was shown that such visual stimulation training is of value as a complementary method in general (first line therapy) [23] as well as for the treatment of therapy-resistant cases (second line therapy) [25]. With this in mind, we have chosen a variation close to the standard crossover design as a method for the present trial, as will be explained in more detail later on (cf. the following section).

The software-implemented exercises for our visual training are based on a specially developed *focal-ambient visual-acuity stimulation* (FAVAS). In the foreground of the screen, a *focal* computer game demands sensory-motor coordination, visual fixation performance, and adherence from the children. Thus, the gaming activity serves mainly for attention binding, which had been previously proven to be a decisive factor for the success of visual-training exercises (Figure. 1). At the same time, an *ambient* stimulation is provided in the game's background by a drifting sinusoidally contrast-modulated grating pattern of constant spatial and temporal frequency. Due to such periodicity, the drifting grating stimulus is assumed to induce resonance within and between filter systems of band-pass selective neuronal transmission channels.

Insert Figure 1 about here

This is relevant since in amblyopia the transmission quality of the *focal* system, which seems to predominantly filter the frequency-modulated neuronal correlates of form perception, appears to be more impaired than that of the complementary *ambient* system for the transmission of spectrally filtered neuronal motion correlates (cf. our discussion section of this paper for more details). Thus, at surface, the amblyopic vision disorder manifests itself in a focal dysfunction of the form channels of high spatial vs. low temporal frequency resolution [20]. Comparatively less disordered appears to be the functioning of ambient motion channels of low spatial vs. high temporal frequency resolution [42]. In light of this, our approach of focal-ambient visual stimulation (FAVAS) is designed to affect the disturbed focal form channels not directly but rather collaterally using the cooperative interplay with ambient motion channels [23, 24, 25].

Objectives

Using this focal-ambient cooperative synergy is crucial for FAVAS, since independently and differing from our above presented approach, the reference to frequency-bandwidth selective visual channels had been already the topic of a very early proposal of supportive amblyopia treatment by grating stimulation. The so-called CAM-stimulator had been developed by the British physiologist Fergus Campbell and his team in Cambridge [9]. Their results were later controversially discussed in view of placebo controlled trials [16, 29, 30, 33, 36]: Because of the unsuccessful replication studies, this attempt was empirically evaluated commonly as a failure.

The Cambridge stimulator aimed at a direct stimulation of form channels, thus, omitting the possible synergy of the motion channels. Its grating stimulus extremely slowly turned clockwise around the center of stimulation, i.e., in a nearly stationary or steady-state way only once per minute around its axis. Therefore, the CAM stimulator was presumably solely based on the proposed influence of spatial frequency selectivity, so there was no significant contribution from the temporal frequency modulation of the stimulus. Accordingly, we proved the question whether this critical feature might have been even the reason for the failure of Campbell's approach which was shown as a result of the above-cited placebo-controlled studies.

In light of this, the main objective of our present investigation was to evaluate the influence of FAVAS visual exercises in combination with standard occlusion *lege artis* with moving gratings (verum condition) as compared to those of sham FAVAS with stationary gratings (control condition) implemented in the background of computer games on the improvement of visual acuity. Thus, our primary outcome consisted in the investigation of the influence of visual exercises using moving gratings as compared to stationary gratings on the development of visual acuity.

As has been recently found, over 90% of amblyopic patients show an astigmatism > 0.5D [50], i.e., this is a very general challenge for treatment. Consequently, meridional amblyopia often arises under astigmatism conditions due to the visual-acuity difference between the differentially affected meridians. In patients with complex visual disorders, it may occur in combination with other forms of functional weakness, such as dysbinocular, anisometropic, or obscuration-related forms. It can also make a significant contribution to the reduction of visual performance in conditions of ocular fundus pathology.

In the present trial, however, it cannot be directly investigated as a primary outcome, since it might only be detected on the base of a post hoc meridional specification of differential influences of verum vs sham excercising *per se*. Therefore, conceived as a secondary outcome, we were to ask for possible differences between the most affected (highest-ametropic) vs. the least affected (lowest-ametropic) meridian in their response to the FAVAS visual exercises in case of meridional amblyopia.

Our hypothesis: FAVAS moving-grating stimulation combined with computer gaming and occlusion is more effective in the maximally ametropic meridian if treating children with meridional amblyopia, than in the minimally ametropic meridian. A comparable difference of this type cannot be expected for a control condition of stationary-grating sham stimulation combined with computer gaming and occlusion.

According to our above declared objectives we aimed, in sum, at the following both outcomes. Primary outcome: best-corrected visual acuity (VA) significantly increases after 10 days of exercising with moving gratings (Verum FAVAS) but not after 10 days of stationary gratings (sham FAVAS). Secondary outcome, being embedded in the result of primary outcome: best-corrected visual acuity (VA) significantly increases in the maximally ametropic but not as much in the minimally ametropic meridian. No changes to the specification of expected primary and secondary outcomes after the trial commenced were introduced in the a priori design.

Patients and methods

Patients

This prospective study adhered to the declaration of Helsinki, and was approved by the local ethics committee (05/2015, trial registration DRKS00022791). This study was conducted at a single center. For this study an informed consent was obtained from patients' legal guardians to take part in the present study, as well as to have the results of this research work published.

Eligibility criteria for participants were prescribed as follows: Sex of the children (male or female), age range between 9 to 14 years old, and the type of amblyopia. As a criterion for the impact we referred to the best corrected visual acuity in each amblyopic eye <0.8 measured by single optical characters. With respect to the type of, patients suffering from amblyopia ex anopsia with astigmatism were chosen, regarding our partial goal of examining effects of meridional amblyopia. No important changes to eligibility criteria were adopted after trial commencement.

Refraction determination in all patients was done under retinoscopy. The best-corrected glasses were then prescribed and worn during the visual exercises.

The random allocation sequence was implemented by the statistician of the Kharkevitch Institute. The method used to generate the random allocation sequence was to grant for comparable variance of both groups by chance. The random sequence was implemented by probabilistically allocated cross-over design. Eligible patients were randomized into two groups, which corresponded approximately to each other in terms of age composition and type of ophthalmopathologic disorder of their visual acuity, i.e. the expression of their respective amblyopia. The patients were allocated to either group in full randomization at 1:1 ratio without any restrictions, e.g., such as blocking.

The participants were assigned to interventions by medical study supervisor Mrs. Rychkova of the Kharkevitch Institute.

The first group consisted of 17 children (34 eyes) aged 10 to 13 (average 11.6 ± 0.3) years. Their mean refractive correction was 4.48 ± 3.58 D absolute sphere with -2.39 ± 1.47 D cylinder by 85,23 ± 76,25 deg for the OD and 4,44 ± 3,86 D absolute sphere with -2,29 ± 1,89 D cylinder by 117,82 ± 70,02 deg for the OS. Of these, 6 patients had myopic astigmatism, 9 patients hypermetropic astigmatism and 2 patients mixed astigmatism. Refractive amblyopia (only against the background of astigmatism) was found in 4 patients, in combination with dysbinocular amblyopia (against the background of strabismus) in 4 patients and in combination with a pathology of the eye background in 7 patients (4 of them were additionally diagnosed with secondary strabismus). Two patients with artiphakia had a combination of refractive and obscuration-related amblyopia.

The second group consisted of 20 children (40 eyes) aged 9 to 14 (average 12.5 ±0.4) years. Their mean refractive correction was 5.57 ± 4.59 D absolute sphere with -1.82 ± 0.92 D cylinder by 72.2 ± 76.24 deg for the OD and 5.75 ± 4.79 D absolute sphere with -1.65 ± 0.99 D cylinder by 98.25 ± 79.80 deg for the OS. Of these, 12 patients had myopic astigmatism, 7 patients hypermetropic astigmatism and 1 patient mixed astigmatism. Refractive amblyopia (only against the background of astigmatism) was found in 3 patients, in combination with dysbinocular amblyopia (against the background of strabismus) in 12 patients and in combination with a pathology of the eye background in 6 patients (in 5 of them a secondary strabismus was additionally diagnosed).

A table is summarizing the main baseline demographic and clinical characteristics for the both groups taken together (Table. 1).

Insert Table 1 about here

All trial participants were patients of a vision training center specialised in the treatment of pediatric eye diseases. Their selection for the present study was based on the criterion that they had previously been newly admitted to the center and had not received any amblyopia treatment in the previous two years. Before that they were intermittently occluded between the ages of 4 and 6 years by their local ophthalmologists. They completed the visual exercises of the study under the direct supervision of the orthoptist-trained pedagogical staff of the vision training center, who also monitored compliance under supervision of their senior ophthalmologist.

Methods

The presented study was planned and carried out as a placebo controlled, double-blinded, randomized trial in cross-over design. According to the prospective design of our study, the variation of the stimulus parameters explored was limited to the above mentioned parametric conditions that proved effective by the previous research [23, 24, 25].

Pre-specifying from these previous studies, we assume that the initial combination of FAVAS with occlusion as a first-line therapy might increase the best-corrected visual acuity by at least two lines over ten days. For the comparison between verum vs. control conditions, we used a certain modification of a crossover design in order to additionally show a possible superiority of first-line therapy application of FAVAS in support of occlusion over a second-line therapy in its application. In light of this, it must be admitted that certainly no washout effect between the cross over training phases can be expected here, as it should be the case in traditional crossover setting. This is since the exercises combined with occlusion are intended to induce a permanent gain of visual function which should be persisting for long time and not decay to zero after the end of training. Therefore, the carry over effect of occlusion is not to be excluded from the design, rather it is well accepted. This is just because we do not compare two kinds of different mono interventions but rather combined interventions: visual exercises with (Verum) or without moving background stimulus (sham) combined with occlusion. Accordingly, we analyze relative differences in accumulated combined effects between both groups with no extensive intermediate washout pausing between phases with different conditions of exercising rather than absolute effects starting from zero after a long intermittent period of washout.

For both groups' exercises, the online vision training (Caterna Vision GmbH, Potsdam, Germany; Amblyocation GmbH, Liebstadt, Germany) was applied in cross-over according to the following two modifications. The first modification of the training program included a concentrically outward-moving grating, before which the computer games took place during stimulation (FAVAS as Verum). The stimulation was carried out at a spatial frequency of 0.3 cyc/deg with the temporal frequency of 1 cyc/sec, resulting in an angular velocity of 3.33 deg/sec. The second modification of the program contained the same grating, with the only difference of being exposed in a stationary (i.e., non-moving) state of presentation (sham-FAVAS as a control condition). In both cases, computer games were played by the children in the foreground of screenplay, which served to bind attention in front of the stimulating grating in the background. The patients trained twice a day for 20 minutes each session. In parallel, the patients received a standard occlusion regimen *lege artis*.

With respect to the above described both conditions, our investigation was planned according to a two-group cross-over design (Figure. 2): The first group of patients initially completed 10 sessions using the moving sinusoidal grating in the background. After a break of one week, the same patients continued their exercises with 10 sessions this time using the stationary sinusoidal grating. In contrast, the second group of patients initially completed 10 sessions with the stationary gratings. After a break of one week, the same patients continued their exercises with 10 sessions this time using the moving sinusoidal grating. All the patients performed in the respective 10 sessions of visual exercises monocularly for 10 minutes for each eye separately.

Insert Figure 2 about here

In accord with our objectives, we examined our patients with regard to their best-corrected visual acuity using a meridionally direction-sensitive visual test inventory especially developed at the Kharkevich Institute [44]. Thereby we estimated the monocular corrected visual acuity in all patients along 4 meridians: 0°, 45°, 90° and 135°. The tests with these visual examinations were carried out before and after the respective 10-days-of-treatment series of our functional amblyopia therapy.

Results

As a result, we plot the mean visual acuity for the both groups of patients at the baseline, after the initially performed training series and after cross over (Figure. 3). Different graphs show effects for the most ametropic meridian vs least ametropic meridian. Additionally, Table. 2 is showing the graphically presented results in their digital representation.

Insert Figure 3 about here

For both groups, the visual acuity was significantly increased only in the stage with a series of exercises with the moving sinusoidal grating. Thereby the visual acuity along different meridians, showed such a statistically significant improvement induced by the moving grating coincident with alignment of the directional optical characters close to the meridian with maximal ametropia (0.27 ± 0.23 to 0.46 ± 0.30 in the first group and 0.39 ± 0.23 to 0.49 ± 0.20 in the second group). No significant improvement was induced by the moving grating in the perpendicular thereto orientation with minimal ametropia (0.38 ± 0.24 to 0.50 ± 0.29 in the first group and 0.46 ± 0.21 to 0.49 ± 0.22 in the second group). After the stage using the stationary grating, however, there was found no statistically significant improvement, regardless of meridian (0.46 ± 0.30 to 0.48 ± 0.29 in the first group for the maximal ametropic meridian and 0.50 ± 0.29 to 0.52 ± 0.28 for the minimal ametropic meridian; 0.36 ± 0.22 to 0.39 ± 0.23 in the second group for the maximal ametropic meridian and 0.46 ± 0.21 to 0.49 ± 0.22 for the minimal ametropic meridian).

Thus, in the measurements of the best corrected visual acuity (BCVA) along four meridians, a statistically significant improvement was found with alignment of the directional optical characters close to the meridian with maximal ametropia, and the minimal improvement in the orientation perpendicular thereto. In the patients of the both groups, the corrected visual acuity had significantly increased as a result of the treatment performed in the stage with a series of exercises with the moving sinusoidal grating only. After the stage of treatment using the stationary grating, however, there was found no statistically significant improvement.

Insert Table 2 about here

For our significant binary outcomes, both absolute and relative effect sizes were calculated. Absolute Cohen's d = 1,91 with a correlation coefficient r of 0.69 for the most ametropic meridian for group 1 with moving gratings (verum) vs. Cohen's d = 0,55 with a correlation coefficient r of 0,27 with stationary gratings (sham). Absolute Cohen's d = 1,09 with a correlation coefficient r of 0,48 for the most ametropic meridian for group 2 with moving gratings (verum) vs. Cohen's d = 0,72 with a correlation coefficient r of 0,34 with stationary gratings (sham).

Discussion

Confirmatory to our preceding trials, the present results show the primary endpoint of aproximately two lines of visual acuity increase in 10 days of 20-minute moving grating FAVAS combined with occlusion, as compared to a stationary grating sham stimulation in crossover. Significant effects were shown to be achieved in the maximally ametropic meridians of patients with meridional amblyopia rather than in the minimally ametropic ones. The greater effect size in the verum condition of group 1 compared to group 2 in crossover seems to indicate that an initial combination therapy of occlusion and FAVAS in the sense of a first-line therapy might be superior to a second-line therapy.

Thus, our home-based therapeutic FAVAS computer games combined with occlusion are shown to be more effective than occlusion without FAVAS even combined with sham stimulation in the presented as well as in the reported earlier trials [23, 24, 25, 32, 37] and therefore promising to overcome the shortcomings of stand-alone occlusion therapy. Therefore, our conclusion of the present results, which we suggest not to be limited exclusively to patients suffering from meridional amblyopia, is that Focal Ambient Visual Acuity Stimulation (FAVAS) in combination with occlusion might be recommended to be applied not only later on, in therapy-resistant cases, but also in all cases of initial amblyopia treatment as early as possible.

There has been lively debate as to whether, in the therapeutic value of FAVAS, the computer games or the stimulating background with moving sinusoidal gratings were the main reason for the visual improvement [5] and whether stimulating approaches should only be used for cases of therapy resistant amblyopia or whether they should also be firstly prescribed from the early beginning as a treatment to newly identified patients from the outset as well. Regarding the critics addressed at these issues of Bau et al [5], however, it must be admitted that the occlusion scheme used in the trial conditions of these authors was adopted directly from Campbell's [9] original proposal prescribing to occlude only within the practice period of visual exercising alone (minimal occlusion). However, in contrast, our objective is a combination therapy of FAVAS together with full occlusion *lege artis*.

Additionally, the results of our present trial strongly demonstrate that the sensory-motor interaction in the computer-gaming activities alone cannot be the main reason for the treatment-induced vision enhancement additional to occlusion since the visual-acuity gain was only obtained in our experimental condition with the moving FAVAS background stimulus grating, but not in our control condition with the stationary background similar to Campbell's [9] approach. This is further underlined by the fact that the maximal gains were selectively addressing the highest refractive meridians and less affecting the lowest refractive ones. Nevertheless, these effects are in no means limited to the specificities of meridional amblyopia alone, since a comparable gain was shown in the earlier FAVAS trials with other forms of refractive and strabismic amblyopia as well [23, 24, 25]. Furthermore, our combination therapy (FAVAS plus occlusion) which shows success with severe astigmatism will be expected even more successful with less severe astigmatism conditions [11, 22].

Discussing these significant effects of moving versus stationary stimulus gratings in comparison to the results of Campbell et al. [9], it must be further premised, that the prototype for our design of the computer-based FAVAS background stimulation was not in as much inspired by the above discussed Cambridge Stimulator *per se*, but rather by a mechanical repetitive-grating arrangement proposed by Haase [18] and Osterloh [38]. This arrangement was originally derived from a visuo-motor and/or visuo-sensor pleoptic stimulation approach which had been developed by Otto and Stangler [40]. Initially, the latter authors described and confirmed in their further related research a beneficial effect of moving light stripe application on the fixation stability of amblyopic eyes [38, 39, 48]. Additionally, Haase [18] and Osterloh [38] found an amplification of this effect using, instead of single bars, a whole grating of repetitively displayed slightly blurred sideward moving light stripes as a background stimulus in a fixation task.

As our preliminary hypothesis, the enhanced treatment effect caused by the spatio-temporal periodicity of the stimulus grating itself is supposed to be achieved as a result of the way the induced optomotoric and optosensoric stimulus effects mutually interact. This is possibly due to a cooperative synergy in the filter characteristics of two systems of different sensory transmission channels [8, 31]. These channels are shown to correspond, roughly speaking, to the neuronal correlates of focal processing of visually perceived form and configurative detail (sustained channels, parvocellular system) versus the ambient processing of motion and rapid change (transient channels, magnocellular system). The filters of each of these channels are selectively tuned to a narrow band of spatial frequencies [7, 10], associated each, as has been found by later research, additionally, with an appropriate temporal frequency range, both constrained to one another in reciprocal, i.e., inversely counterbalanced synergy [26, 27].

This interdependence is supposed to bear on a certain kind of non-linear coupling in the synchronisation of brain functioning by means of so-called neuronal synfire-chains [1, 2]. According to this view, the drifting light stripe stimulation under spatial and temporal periodicity of a limited frequency bandwidth (which characterizes spiral patterns, e.g., as the ones of pleoptic centrophor exercises by Bangerter [4] und Cüppers [12] too) is applied to the disturbed synfire-chain system's dynamics as an externally organizing order parameter. Thus, it is expected to support regaining the internal temporal coherence of normally highly ordered cortical processing loops which were shown to be desynchronised, however, in amblyopia [15, 28, 43].

Therefore, in addition to the originally reported fixation-stabilizing optomotoric effect of the pleoptic light stripe stimulation [38, 39, 40, 48], we suppose the repeated stripes [18; 38] in the drifting sinusoidal grating to further induce another useful effect: i.e., of optosensoric resonance in complementary banks of bandwidth selective filters of form vs. motion channels due to their cooperatively intertwined mode of visual processing. According to our preliminary hypothesis, the internal cortical synchronisation in brain areas being addressed by the focal macular form channels of the central retina is probably externally supported, i.e., via resonant phase coupling to oscillations from brain areas addressed by ambient motion channels in the peripheral retina [24, 25].

Another treatment sharing some common theoretical fundamentals with the spatial-frequency approach of Campbell`s as well as to our proposed stimulation has been developed and verified in placebo-controlled trials by Polat et. al. [41]. In their "perceptual-learning" training, high-contrast ambient grating stimuli in a collineated arrangement of Gabor patches are used as peripheral flankers inducing some focal detection enhancement of low-contrast central Gabor patches of common spatial frequency. Their studies demonstrated a considerable efficacy of such training for the improvement of contrast sensitivity and visual acuity in adult amblyopic patients. In common with Campbell`s and our approaches, Polat`s training is also based on the assumption of an ambient frequency-selective cooperative effect of peripheral retinal stimulation on central retinal low-level focal visual processing. However, similar to Campbell's and differing from our proposed stimulus arrangement, in Polat's setting the peripheral influence on central vision was mediated by stationary, not by moving stimuli, thus, an influence of spatial frequency on visual learning in their conditions only may be predicted, thereas a such of time frequency is certainly excluded. Additionally, differing from Campbells and our approaches, Polat's training is based on a detection task with respect to the presented Gabor low contrast grating macular stimulus, which might be easily coped with by adults, but might be tedious to children.

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Declaration of Interest

The corresponding author is scientific consultant of Caterna Vision GmbH and Shareholder of Amblyocation GmbH

He has the right to post this manuscript and confirm that all authors have assented to posting of the manuscript and inclusion as authors.

The authors confirm all relevant ethical guidelines have been followed, and any necessary IRB and/or ethics committee approvals have been obtained. They are legally responsible for the content of the article.

All necessary patient/participant consent has been obtained and the appropriate institutional forms have been archived.

The authors understand that all clinical trials and any other prospective interventional studies must be registered with an ICMJE-approved registry, such as ClinicalTrials.gov. They confirm that such study reported in the manuscript has been registered and the trial registration ID is provided.

Tables

Table 1: Patients' characteristics

Age			
	Range	Mean	SD
	9 - 14	11,2	± 0,4
Gender			
	male	female	
	27	10	
Amblyopic Eye			
	left	right	
	37	37	
Type of amblyopia			
	strabism	refraction	both
	36	28	10
Geometric mean of visual acuity of both groups before treatment			
	Maximal ametropic meridian visual acuity	Minimal ametropic meridian visual acuity	
	0,29 ± 0,26	0,40 ± 0,26	

Table 2: Mean visual acuity results for the both groups of patients. Significance revealed by independent t-Test is marked by double asterisk (p<0.05).

Means of best corrected visual acuity Group 1	**Pre treatment**	**After 10 days of treatment with moving gratings**	**After 10 days of stationary gratings**
	1	**2**	**3**
Visual acuity in the most ametropic meridian	0.27 ± 0,23	0.46 ± 0,3 **p(1-2)= 0.046****	0.48 ± 0.29 p(2-3) = 0.822
Visual acuity in the least ametropic meridian	0.38 ± 0.24	0.5 ± 0.29 p(1-2) = 0.084	0.52 ± 0.28 P(2-3) = 0,82
Means of best corrected visual acuity Group 2	**Pre treatment**	**After 10 days of stationary gratings**	**After 10 days of treatment with moving gratings**
	1	**2**	**3**
Visual acuity in the most ametropic meridian	0.36 ± 0.22	0.39 ± 0.23 p(1-2) = 0.63	0.49 ± 0.2 **P(2-3)= 0.04****
Visual acuity in the least ametropic meridian	0.46 ± 0.21	0.49 ± 0.22 P(1-2) = 0.52	0.54 ± 0.21 P(2-3) = 0,32

Figure Captions

Figure 1: Example of FAVAS Stimulation in the background and finished game for adherence in foreground.

Figure 2: Patients' allocation over trial conditions

Figure 3: Mean decimal visual acuity results for baseline and treatment before vs. after cross over

Figures

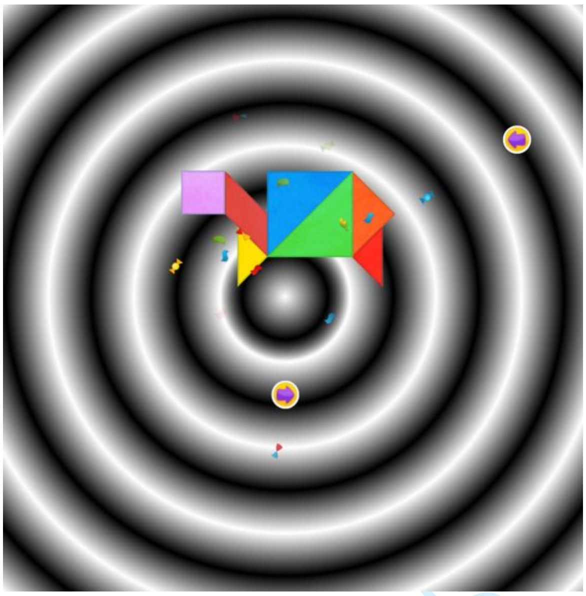

Figure 1

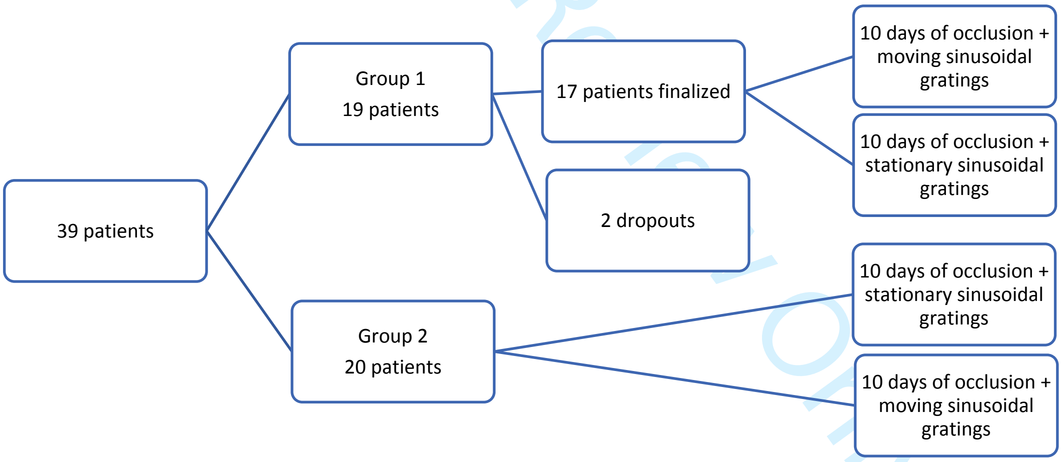

Figure 2

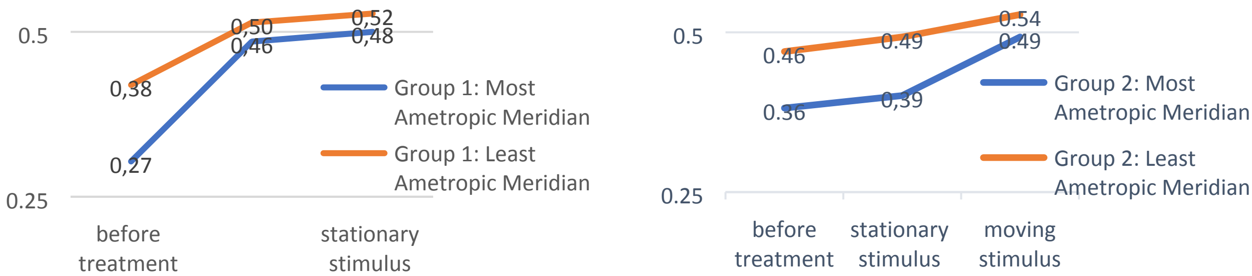

Figure 3