TREATMENT OF UNILATERAL AMBLYOPIA. COMPARISON OF METHODS CAM (CAMPBELL VISION STIMULATOR) AND CRCS (COLOUR REVERSAL CHECKERBOARD STIMULATION OF RETINA)

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SUMMARY

The authors evaluate the effectiveness of new method – Color Reversal Checkerboard Stimulation of the retina (CRCS) in the treatment of unilateral anisometropic amblyopia in group of total 157 children followed during the period 2008–2012 at the Department of Pediatric Ophthalmology, University Hospital and Masaryk University in Brno. The authors evaluate the improvement in best corrected visual acuity in groups of children with myopic and hyperopic anisometropia and compare the effectiveness of CRCS with a commonly used pleoptic method Campbell visual stimulator.

Authors introduce an original method in the amblyopia treatment suitable to upgrade current methods of pleoptics.

Key words: CAM, amblyopia, anizometropia, color reversal checkerboard stimulation of retina CRCS

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INTRODUCTION

Despite all endeavours to ensure timely diagnosis through a programme of preventive eye examinations, amblyopia remains one of the frequent causes of permanent loss of sight after the age of 9 years in children. After this age, in most cases there is practically no possibility for therapeutic improvement of the best corrected visual acuity (BCVA). On the basis of current statistics, every 12th child at the age of 4 years has an undetected ocular defect, the late identification of which may have lifelong consequences (2). One of the most frequent causes of amblyopia is anisometropia.

Tried and tested methods of pleoptic exercise using instruments have been used over the long term for the treatment of amblyopia. In recent years, on a background of advance in the field of information technologies, new possibilities have opened up for stimulating the retina and visual pathways at an early age. These advances extend the options for pleoptic therapeutic methods, and may contribute to a reduction of the incidence of amblyopia in the child population.

One of the original methods of passive pleoptics remains treatment with a Campbell vision stimulator (CAM). The method uses checkerboard circles with progressively reducing identical black and white fields. The instrument contains 7 discs, of which each disc is rotated for 1 minute.

The CAM method, in which identical sizes of fields are alternated within an identical time, is the basis for the original semi-automatic computer program of colour reversal checkerboard stimulation of the retina (CRCS). The new method is based on stimulation of the retina by contrast, but instead of black-white reversal the CRCS method uses red and green colours. This therefore causes stimulation of the retina not by means of a contrast in brightness, as is the case of the CAM method, but by reversal of sharp-edged coloured fields. In amblyopic patients it is possible to presuppose a higher effectiveness of stimulation of the central part of the retina by colour stimulus.

The aim of the study is a prospective evaluation of the efficacy of the original method of CRCS in the therapy of unilateral anisometric amblyopia in children, and a comparison with the CAM method.

METHOD

The study observed a total of 157 children treated at the Department of Paediatric Ophthalmology at the University Hospital and Faculty of Medicine at Masaryk University in Brno. Data obtained through prospective processing of the results of two cohorts of patients was analysed. The first group of patients comprised 105 children with myopic anisometropia, and the second group comprised 52 children with hypermetropic anisometropia. All 157 children had unilateral anisometropic amblyopia and good vision in the other eye (BCVA 1.0). The average age at the time of commencement of therapy was 4.7 years (range 4-7 years). All the children in the cohort had full correction of the spherical and cylindrical component of a refractive error in the amblyopic eye by means of glasses or contact lenses, or a combination thereof according to the type and size of the dioptric defect. Both cohorts of paediatric patients were comparably represented in terms of sex, and had an identical pleoptic therapeutic procedure (full correction of refractive error, occlusion therapy 6 hours per day and identical motivation strategy with repeated interviews). Both groups were further divided according to the used method of treating amblyopia, into a sub-group for therapy using the pleoptic method CAM and a sub-group for treatment with CRCS. The patients were divided into sub-groups at random and the period of duration of pleoptic exercise was 1 hour per week twice for all patients. The pleoptic exercise took place at the Pleoptic and Orthoptic Section of the Department of Paediatric Ophthalmology at the University Hospital and Faculty of Medicine of Masaryk University in Brno, and a vision test was always performed before the pleoptic exercise. The pleoptic exercise was finished upon a stabilisation of vision of the amblyopic eye at a value of 5/5 without a decline after the subsequent four follow-up examinations or when the child reached the age of 9 years, and/or upon no improvement of amblyopia over a period of 3 months.

Colour reversal checkerboard stimulation of the retina (CRCS)

This is an original semi-automatic computer program. The new method is based on stimulation of the retina by contrast as in the CAM method, in which identical sizes of fields alternate in an identical time, but instead of black-white reversal, the CRCS uses red and green colours. The CAM method stimulates by means of a contrast of brightness, as against which the method of CRCS uses reversal of sharp-edged coloured fields. If the luminance of both colours is the same, it is possible to differentiate contrast of colour from contrast of brightness. Isoluminance can be verified for example by placing one used colour on one half of the monitor, and simultaneously placing the second (complementary) colour on the remaining half of the monitor. Upon simultaneous projection of both colours, it is then possible to use a regular lux meter or more optimally a (calibrated) absolute radiometer in order to verify that both coloured halves of the monitor radiate the same amount of light energy.

The patient sits at a distance of 1.0 metre from a 17‘ monitor. A central symbol is fixed, which can be modified according to initial vision and the age of the patient in terms of size and motif. For a period of 1 minute the patient observes the red-green colour reversal with the largest fields, which after the elapse of this period are replaced by smaller fields. Over a total period of 7 minutes, 7 sizes of checkerboards alternate, with various spatial frequencies. The colour intensity remains the same throughout the entire period. For better maintenance of attention of the child patient, it is possible to change the fixation symbol during the course of the exercise or during the course of the entire period of therapy. A symbol in the form of an image may be replaced with another symbol of identical size. As in the case of the CAM method, it is also possible to discontinue and recommence the stimulation at any time, and to follow on from an already completed series. The wavelength of colours is selected in such a manner as to ensure that the stimulation copies as well as possible the peripheral colours of the spectrum, and upon reduction of brightness then approaches black and white, as an elimination of stimulation only by contrast.

Size of central fixation symbol

Images in the centre of the monitor, in a square whose thickness (of entire symbol) is equal to 1/5 of its height, in order to adhere to the minimum separabile of one angular second at a distance of one metre, from which the patient observes the monitor according to the formula $\mathrm{tg}\,(1°/3600'') = x / 1\,000\,000\ \mu m$. $x = 4.84\ \mu m$. Therefore, upon vision of 1.0, the fixation symbol is a square with a side of 5 µm, which would apply for stimulation of the foveola. Such a small symbol would be very difficult to construct on a PC if we wished to stimulate the foveola itself. Upon stimulation of the fovea centralis and perifoveal region, the fixation symbol may therefore be larger.

Before each running of the program, manual calibration of the monitor is performed in order to ensure consistent configuration of the size of the squares. Configuration of the image to central fixation, of its type (symbol, image) and size is possible. Red and green colour with amateur colour calibration using a Nokia test (www.softcom.cz/eshop/nokia-monitor-test_d8209.html) is configured in such a manner as to correspond in its intensity identically on all available colour monitors.

RESULTS

The average observation period throughout the entire cohort of 157 patients was 3.76 ± 1.45 years. The patients were divided into groups according to the type of anisometropia and subsequently by random selection according to the type of pleoptic method. The distribution of patients is presented in detail in table 1.

Results of treatment of unilateral amblyopia in the group of children with myopic anisometropia

105 children with myopic anisometropia treated for unilateral amblyopia were divided into group A (48 children treated by CAM method) and group B (57 children treated by CRCS method) (see table 1).

The average age in the group of children with myopic anisometropia at the time of commencement of therapy was 4.7 ± 2.1 years (range 4-7 years), and did not show statistical significance between both groups (A, B) (table 2).

The average period of duration of treatment in the group of children with myopic anisometropic amblyopia treated

Table 1. Division of 157 children into groups according to type of anisometriopic amblyopia and used pleoptic

Group	Number of children total	Number of children treated by CAM method	Number of children treated by CRCS method
Myopic anisometropia	105	48 (group A)	57 (group B)
Hypermetropic anisometropia	52	24 (group C)	28 (group D)

CAM – Campbell visual stimulator
CRCS – Colour reversal checkerboard stimulation of the retina

with CAM and CRCS was 9.8 and 10.7 months respectively; the average value of spherical refractive error in cycloplegia in the entire group of 105 children with myopic anisometropia was -7.37 dsf (range -9.0 to -4.0 dsf). The difference in the average values of refractive error, initial BCVA and length of duration of treatment did not show any statistically significance between both groups (A, B) (table 2).

In group A (children with myopic anisometropic amblyopia treated by CAM), average initial BCVA in the blunt-sighted eye before treatment was 0.21 ± 0.19 (range 0.1 – 0.4), and after treatment the average final value of BCVA was 0.62 ± 0.13 (range 0.3-0.9) (table 2).

In group B (children with myopic anisometropia treated by CRCS), average initial BCVA before treatment was 0.24 ± 0.17 (range 0.05 to 0.4) and after treatment average final BCVA was improved to 0.93 ± 0.11 (range 0.6 to 1.0) (table 2).

The difference in the average values of final BCVA at the end of the observation period between both groups (A and B) was statistically significant; p = 0.0172. The improvement of average BCVA in the group of children with myopic anisometropia treated by CRCS was greater in comparison with the group of children treated by CAM (0.93 v 0.62) (table 2).

Results of treatment of unilateral amblyopia in the group of children with hypermetropic anisometropia

52 children with hypermetropic anisometropia treated for

Table 2 Results of treatment of unilateral amblyopia in group of children with myopic anisometropia. Comparison of CAM v CRCS

Parameters:	CAM Group A (48 children)	CRCS Group B (57 children)	P value
Refraction in cycloplegia Spherical defect in a.e. average ± SD (range)	-7,38 ±1,83 (-4,50 až -9,00)	-7,23 ± 1,91 (-4,75 až -8,50)	0,281
Astigmatism in a.e. average ± SD (range)	-1,32 ± 1,14 (-0,50 až -3,25)	-1,43 ± 1,27 (-0,25 až -3,75)	0,367
BCVA in a.e. before treatment average ± SD (range)	0,21 ± 0,19 (0,1 - 0,4)	0,24 ± 0,17 (0,05 - 0,4)	0,415
BCVA in a.e. after treatment average ± SD (range)	**0,62 ± 0,13** (0,3 - 0,9)	**0,93 ± 0,11** (0,6 - 1,0)	**0,0172 ***
Age at time of beginning of treatment (years) average ± SD (range)	4,8 ± 2,1 (4 -7)	4,6 ± 1,9 (4 - 7)	0,291
Duration of treatment (months) average ± SD (range)	9,8 ± 1,2 (7 -14)	10,7 ± 1,3 (7 - 14)	0,341

*P < 0.05 statistically significant; Student T-test
SD – standard deviation, a.e. - amblyopic eye, CAM – Campbell vision stimulator, CRCS – colour reversal checkerboard stimulation of the retina, BCVA – best corrected visual acuity.

Table 3 Results of treatment of unilateral amblyopia in group of children with hypermetropic anisometropia. Comparison of CAM v CRCS methods on 52 children.

Parameters:	CAM **Group C (24 children)**	BRS **Group D (28 children)**	P value
Refraction in cycloplegia Spherical defect in a.e. average ± SD (range)	+3,62 ±1,87 (+1,75 až +5,50)	+3,78 ± 1,64 (+1,75 až +5,75)	0,419
Astigmatism in a.e. average ± SD (range)	+1,13 ± 0,96 (+0,25 až +2,50)	+1,21 ± 0,86 (+0,50 až +2,25)	0,306
BCVA in a.e. before treatment average ± SD (range)	0,13 ±0,11 (0,1 - 0,3)	0,18 ± 0,12 (0,1 – 0,4)	0,297
BCVA in a.e. after treatment average ± SD (range)	**0,53 ± 0,22** (0,3 - 0,7)	**0,89 ± 0,16** (0.5 - 1.0)	**0,00197 ***
Age at time of beginning of treatment (years) average ± SD (range)	4,6 ± 2,3 (4 – 7)	4,4 ± 1,9 (4 - 7)	0,331
Duration of treatment (months) average ± SD (range)	10,2 ± 1,4 (7 – 14)	10,8 ± 1,6 (7 – 14)	0,453

*P < 0.05 statistically significant; Student T-test
SD – standard deviation, a.e. - amblyopic eye, CAM – Campbell vision stimulator, CRCS – colour reversal checkerboard stimulation of the retina, BCVA – best corrected visual acuity.

unilateral amblyopia were divided into group C (24 children treated by CAM method) and group D (28 children treated by CRCS method) (table 1).

The average age in the group of children with hypermetropic anisometropia at the time of commencement of therapy was 4.5 ± 2.1 years (range 4-7 years), and did not show statistical significance between both groups (C, D) (table 3).

The average period of duration of treatment in the group of children with hypermetropic anisometropic amblyopia treated with CAM and CRCS was 10.2 and 10.8 months respectively; the average value of spherical refractive error in cycloplegia in the entire group of 52 children with hypermetropic anisometropia was +3.75 dsf (range + 1.75 to +5.50 dsf). The difference in the average values of refractive error, initial BCVA and length of duration of treatment did not show any statistically significance between both groups (C, D) (table 3).

In group C (children with hypermetropic anisometropic amblyopia treated by CAM), average initial BCVA in the blunt-sighted eye before treatment was 0.13 ± 0.11 (range 0.1 – 0.3), and after treatment average final value BCVA was improved to 0.53 ± 0.22 (range 0.3 to 0.7) (table 3).

In group D (children with hypermetropic anisometropia treated by CRCS), average initial BCVA before treatment was 0.18 ± 0.12 (range 0.1 to 0.4) and after treatment average final BCVA was improved to 0.89 ± 0.16 (range 0.5 to 1.0) (table 3).

The difference in the average values of final BCVA at the end of the observation period between both groups (C and D) was statistically significant; p = 0.00197. The improvement of average BCVA in the group of children with hypermetropic anisometropic amblyopia treated by CRCS was greater in comparison with the group of children treated by CAM (0.89 v 0.53) (table 3).

DISCUSSION

The problem of treatment of anisometropic amblyopia resides first and foremost in its late diagnosis. In contrast with visually perceptible amblyopia in the case of strabismus for example, anisometropic amblyopia is often detected later in children. Even a high refractive error may remain for a long time unidentified and uncorrected, and the severity of amblyopia may reach surprising levels. Studies demonstrate a correlation between a higher degree of anisometropia and a higher prevalence and severity of amblyopia (5, 8, 10, 11). Important factors influencing the results of treatment of blunt-sightedness represent the age upon determination of the error, age at the time of commencement of treatment and BCVA at the time of commencement of treatment (5, 7). Hussein et al. (4) determined initial BCVA in the amblyopic eye of 0.1 or worse as a significant risk factor of failure of treatment. This points to the fact that in the conditions of persistence of high amblyopia, abnormal binocular interactions and/or visual deprivations occur. Choi and Kim (6) highlight the importance of the co-operation of the patient and their family in the treatment of amblyopia. The effect of occlusion therapy has been demonstrated by several studies (1, 11).

Classic methods of pleoptics include the method of Campbell vision stimulator (CAM). The CAM method was based on the discovery that the neurones of the brain stem respond well to lengthwise contrast stimuli with a certain orientation, moving in a certain direction and at a certain speed. The instrument is composed of inclined plates, onto which circular discs are placed with a checkerboard containing fields of various sizes. In Campbell's original design these were black and white stripes, which were later replaced with a checkerboard, which better stimulates the visual cortical neurons (3). This method stimulates the central and peripheral retina through the modality of change of contrast and movement.

The new method of colour reverse checkerboard stimulation of the retina (CRCS) is based on stimulation of the retina by contrast, as in the CAM method, but instead of black-white reversal it uses red and green colours. This therefore causes stimulation of the retina not by means of a contrast in brightness, as is the case in the CAM method, but by reversal of sharp-edged coloured fields. In amblyopic patients it is possible to presuppose a higher effectiveness of stimulation of the central part of the retina by colour stimulus.

Both CAM and CRCS techniques stimulate the lowest levels of vision systems. CAM stimulates the parvocellular pathway by means of an extremely high right-angled contrast of brightness, then according to the size of the squares, first of all the magnocellular pathway and then, upon a reduction of the fields also the parvocellular pathway, whilst the rotation movement stimulates the magnocellular pathway. CRCS stimulates the parvocellular pathway purely and intensively by means of colour contrast, without a contrast in brightness. This is probably the main reason for the effectiveness of this procedure in increasing BCVA. These considerations are based on a separation of the associative areas (V3 and above – higher visual cortex area) and in part also the perceptual (retina, corpus geniculatum laterale and entrance to V1 – area 17) and analytical components (V1 – area 17 and V2 – area 18) into the “colour blind” magnocellular system (perception of movement, low contrast and dynamic shape) and the colour-perceiving parvocellular system (perception of colours and high contrast). The parvocellular pathway corresponds to modulation in the dimension of green/red. As against this, the magnocellular pathway corresponds best to modulation within the dimension light/dark (8).

CONCLUSION

The new method of the colour reverse checkerboard stimulation of the retina represents an effective treatment of amblyopia. In comparison with the pleoptic method of the Campbell vision stimulator, it improves best corrected visual acuity of the blunt-sighted eye more effectively in the group of children with both myopic and with hypermetropic anisometropia. The method of colour reverse stimulation of the retina can be used for the innovation of current methods of pleoptics.

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