ORIGINAL ARTICLE

Visual reaction times in strabismic amblyopia: a case-control study

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Abstract. *Background:* Visual reaction times (RT) have been used for the evaluation of the response to visual stimuli in amblyopic subjects in a case-control study. *Materials and Methods:* A Study Group, consisting in nine subjects with amblyopia and anomalous retinal correspondence, and a Control Group of nine normal subjects, were examined. In order to measure RT a test was carried out using a personal computer, for generating the visual stimuli on a special 14" monitor and for recording the response. A program was specifically created to record the dimensions of the stimuli and times of presentation in milliseconds. An electrographic tracing controlled the visual fixation. Visual stimuli of different dimensions were presented to the amblyopic eye, the dominant and non dominant eye, and in binocular vision, and RT were recorded. *Results:* In all cases RT represented a decreasing function of the stimulus dimension, with no statistical difference between the two groups (p=0,471). In both groups, RT values deriving from the greatest stimuli were rather inferior to those measured with smaller stimuli (p<0,001). In the Study Group the same stimulus produced longer reaction times in the amblyopic eye compared with those of the dominant eye (p<0,001), as well as those recorded during binocular vision (p<0,001). *Conclusions:* RT to visual stimuli could supply objective information on uncertain or hidden amblyopia. The extension of the experimental protocol to a larger population under school age could provide a clinical application for the early diagnosis of sensory alterations. (www.actabiomedica.it)

Key words: Amblyopia, anomalous retinal correspondence, visual reaction times, binocular vision

Introduction

Visual reaction times (RT) have been used for the evaluation of response to visual, auditory, and tactile stimuli, in both normal and pathological conditions (1). Simple RT have shown a better response in binocular vision in normal subjects than in vision of a single eye (2), and this means, to a certain extent, that the difference of performances could be somehow related to the degree of binocular summation. To our knowledge, a few studies have been devoted to RT in strabismic amblyopia or in anomalous retinal correspondence (ARC). A longer lag phase or latent period in the visual reaction times of the amblyopic eye could have been shown in two studies: one with three subjects (3) and the other one with a larger number of subjects (25 normal, 36 strabismic) but with no variation in the extent of the applied stimulus (4). A similar result appeared at different spatial frequencies in amblyopic subjects (5).

We have measured the latency of the response in subjects with amblyopia and anomalous retinal correspondence. We also considered the comparison of the responses between dominant and non dominant eye. In addition, we aimed at verifing the occurrence of binocular summation during the measurement of visual reaction times to visual stimuli in normal subjects and subjects suffering from strabismic amblyopia with anomalous retinal correspondence, as found and described in electrophysiological studies (6, 7).

Materials and Methods

Apparatus and Stimuli

The test was carried out using a 486 IBM personal computer, for generating the visual stimuli on a special 14” monitor and for recording the response. Stimuli were displayed on a VGA monitor with P22 phosphor of an IBM-compatible PC, which generated the stimuli and recorded the responses.

The chin-rest, the monitor - on which the light stimuli were generated - and the response button were placed in an acoustically isolated room which was illuminated with a soft light.

The chin-rest was positioned so that the median point between the eyes of the subject was lined up with the central point of the screen, which was placed 57 centimeter from the subject. Given such experimental conditions, an object of one centimeter in length on the monitor subtended a visual angle of 1°, according to the following formula:

visual angle $\alpha°$ = (object dimensions in centimetres x 57.296)/distance of the object in meters

The program for generating the stimuli was specifically created to record the dimensions of the stimuli and times of presentation in milliseconds.

Square-form stimuli were produced in the center of the monitor. The square-form stimuli had four different sizes: 2 cm squared (S-2), 1 cm squared (S-1), 0.5 cm squared (S-0.5) and 0.25 cm squared (S-0.25), equivalent to visual angles of 2°, 1°, 0.50° and 0.25°, respectively. These dimensions respectively corresponded to the following values of visual acuity: 2°= 20/800; 1°= 20/200; 0.50°=30’=20/100; 0.25°=15’=20/50.

The duration of presentation for each stimulus (imperative stimulus) was 150 milliseconds.

The stimulus was repeated 20 times for each dimensional level, according to a random sequence in the program for a total number of 80 tests. The sum of the 80 presentations was called “block”. There were 3 blocks for each subject: in monocular vision with the dominant eye, in monocular vision with the non dominant eye (or with the amblyopic eye), and in binocular vision.

The background monitor lighting was equal to 31.5 apostilbs, while stimuli had a lighting of 315 apostilbs.

When the square stimulus was not shown, there was a 5 mm bright cross (315 apostilbs) in the center of the screen to keep the subject staring at it.

The subjects were told to keep staring at the cross and to notice the presentation of the imperative stimulus by pressing a button. The subjects were also told to answer as quick as possible. The answer time was automatically measured and recorded by the computer.

Thus, every single test was made up of 3 main successive stages: Stage 1: the cross was in the center of the screen; Stage 2: the square-form stimulus overlapped the cross; Stage 3: disappearance of the stimulus, only the cross was visible along with RT in milliseconds.

The bright stimulus overlapped the cross with a random lag phase or latent period between 100 and 400 milliseconds (ms). The beginning of each test was signalled by the presentation of the cross, which was followed by the imperative stimulus, after a randomly varying interval between 100 and 400 ms. Such a variability was introduced to prevent the anticipation of the answer as the examination went on (training effect).

Each test time was shown on the monitor, both as a kind of reward and in order to keep the subject concentrated on it.

Thanks to the insertion of two cut-off values, the program automatically refused responses inferior to 100 ms and superior to 500 ms. In fact, the responses inferior to 100 ms were certainly given in advance, while those superior to 500 ms were more voluntary than instinctive responses; the latter show that the subject was distracted and did not answer quickly enough to the visual stimulus.

For the control of the visual fixation, an electrographic tracing was used, through the application of two electrodes on the temporal area and one on the ear lobe. An operator checked the fixation through the entire test: oscillations up to 10 mm from the fixation point were accepted as equivalent to 1° of visual angle; if the oscillations exceeded such limits the response was refused.

Apart from the decreasing fixation, other errors were taken into consideration: anticipated response, that is, given before the presentation of the stimulus; response posterior to the presentation of the stimulus, but anticipated as being inferior to the best obtainable answer (100 ms); postponed response beyond the fixed limits (500 ms).

The system recorded the errors and presented the stimuli related to the wrong responses. Thus, the test was complete with 80 right responses for each block.

Subjects

The protocol was based on two groups of subjects: the Study Group: subjects suffering from esotropia with strabismic amblyopia and ARC; and the Control Group: normal subjects.

The study adhered to the Tenets of the Declaration of Helsinki. The criteria for inclusion in the two groups are the following:

for the Study Group: age between 20 and 30 years; best corrected visual acuity (BCVA) of 20/20 for the dominant eye; BCVA of the amblyopic eye between 20/200 and 20/32; angle of deviation in convergence between 6 and 20 prism dioptres; ARC at the Bagolini Striated Glasses (8); suppression scotoma in the binocular visual field detected with the Binocular Polaroid Test (9; 10); absence of anisometropia; absence of eccentric fixation; normal dioptric conditions and fundus.

For the Control Group: age between 20 and 30 years; BCVA of 20/20 in both eyes; absence of heterophoria or history of previous ocular motility disturbances; absence of anisometropia; normal dioptric means and fundus.

Amblyopic subjects were identified among those examined over the last year in the Unit of Ophthalmology. Nine subjects accepted to undergo the test. Normal subjects were recruited among the medical and paramedical staff of the same Unit. All the subjects were informed about the formalities and finalities of the test. Moreover, they were asked to sign a consent for their inclusion in the study as well as for the privacy of the collected data.

Therefore, all subjects underwent a complete ophthalmological examination, which included: measurement of BCVA; ocular motility examination; slit-lamp biomicroscopy; fundus oculi, particularly referred to the macula and optic disc; ocular dominance (alignment test).

Only the subjects with visual acuity in the amblyopic eye of 20/200 or more (BCVA≥20/200) were included in the Study Group, thus they could see the four dimensions of the test stimulus.

We considered anisometropia as a difference of refraction in spherical equivalents (SE) between the two eyes that exceeded 1.5 diopters.

The presence of the eccentric fixation was derived from the data collected by previous evaluations, and was confirmed using a retinoscope.

BCVA was measured through ETDRS chart: the value corresponding to the first line in which the subject gave two wrong answers on 5 presentations was used as a measure of the visual acuity.

The strabismic deviation was measured for distant fixation with prism cover test.

We examined the anterior segment and fundus oculi in miosis.

The ocular dominance in the subjects included in the control group was assessed through the alignment test. The test consists in asking the subject to line up two vertical sights according to the common visual direction, alternating the right eye with the left eye. The subject has to assess with which eye the alignment can be seen, which is the dominant eye.

The subjects underwent the experimental test at the Unit of Human Physiology of the University of Parma. Previously, they filled out the Oldfield questionnaire for the determination of manual preference (11).

Apart from 2 left-handed subjects in the study group, the remaining subjects were right-handed.

Procedure

The subject sat in front of the monitor, with the index finger of the preferred hand, according to Oldfield's quotient of laterality (11), on the answer button. Before recording the "real" answers, the examiner showed 40 stimuli, as a kind of warm-up, illustrating the characteristics and describing the possible mistakes in the answers. At the end of this first phase, the recording began. The test was performed with the best optical correction.

For each subject, 3 blocks of tests were carried out: 1 block for the dominant eye (closing the other eye); 1 block for the amblyopic/non-dominant eye (closing the other eye); 1 block in binocular vision.

At the end of each block the subject rested for 2 minutes. It took 6 minutes to carry out each test, both for the amblyopic subject and for the other subjects.

Since all subjects carried out 3 blocks of tests, a learning effect was expected. If the reaction times are for the amblyopic eye, measuring its response before the dominant eye would mean inducing an increasing difference between the two eyes. Similarly, examining the dominant eye first and then the amblyopic eye could reduce such difference. The possible learning factor had to act on all the groups without helping or opposing one of them. Therefore a random presentation of the stimuli was chosen.

The experimental device which met with these needed requirements was the balancing technique of Latin square, a matrix with a number of lines and columns corresponding to one of the procedures of presentation, that is 3x3. Each element of the square was marked by a letter; all the elements occurred just once in every line and column, according to the following scheme: A = presentation to the dominant eye; B = presentation to the amblyopic / non dominant eye; C = binocular presentation.

Consequently, the square will be:

A	B	C
C	A	B
B	C	A

corresponding to the 3 sequences of presentation.

In both groups these sequences were given to subgroups of three subjects.

At the end of the 3 blocks of tests we had 240 answers (in milliseconds) for each subject, that is, 80 answers for the 3 types of test (dominant eye, amblyopic/non dominant eye, binocular). The 80 answers were subsequently divided into four subgroups, corresponding to the different dimensions of the stimulus, thus obtaining 20 answers for each type of stimulus.

Statistical analysis

For the statistical analysis, the following parameters were taken into consideration: age (expressed in years); BCVA expressed in *20ths* (ETDRS) for the description of the sample characteristics and in logMAR for the statistical calculations; refraction, expressed in SE; strabismic deviation for distant fixation, expressed in prism diopters.

The average results of the 80 answers for each block of tests have been listed according to the procedures of presentation and the dimensions of the visual stimuli, as follows: DOM for the answers given by the dominant eye (both groups); AMB for the answers given by the amblyopic eye (study group); NDOM for the answers given by the non dominant eye (control group); BIN for the answers derived from binocular vision (both groups); S 0.2 for the 0.25° stimulus; S 0.5 for the 0.50° stimulus; S 1 for the 1° stimulus; S 2 for the 2° stimulus.

The computer program calculated the average value of RT in milliseconds.

The average and standard deviation (SD) of the variables taken into consideration (age, dominant eye refraction, amblyopic/non dominant eye refraction, visual acuity expressed in logMAR, and strabismic deviation in the Study Group) were calculated through the statistic program SPSS 9.0. Similarly, the average RT for each dimensional level of the stimulus and for each procedure of presentation was calculated. The average RT for the 4 dimensional levels was referred to the above parameters through the linear regression test. The average RT for the different procedures of presentation and for the different dimensional levels of the stimulus was compared through the Student-t Test for single data and the Variance Analysis Test (ANOVA). For every dimensional level and for each procedure of presentation the average RT was compared. They had previously been derived from the subjects from the two groups through the Student-t Test for coupled or paired data and the ANOVA Test: statistical analysis among groups.

Particularly, the 3-factor ANOVA Test was applied as follows: a factor among subjects or “between-subjects”, represented by the factor group (Study -

Control); two factors "within-subjects", represented by the eye variables (dominant, amblyopic / non dominant eye, binocular) and the stimulus dimension respectively (S 0.2, S 0.5, S 1, S 2).

If necessary, post-hoc analyses were performed through the Newman-Keuls method.

Results

The Study Group included 9 male subjects, aged 26,56±3,3 years (mean±SD, range 20-29), 7 right-handed and 2 left-handed. Amblyopic eye was the right eye in 3 cases and the left eye in 6 cases: both of the left-handed subjects had an amblyopic left eye. BCVA of the amblyopic eye, expressed in logMAR, was 0,51±0,25 (mean±SD, range 1-0,2); best optical correction was +2,16±1,8 SE (mean±SD, range +2/+5). BCVA of the dominant eye was logMAR 0,0 in all cases, with the best optical correction of +1,38±1,53 SE (mean±SD, range +1/+4). Strabismic deviation of the amblyopic eye was +7,88±3,1 prism diopters (mean±SD, range +6/+14).

The Control Group included 9 subjects, 3 males and 6 females, aged 28,56±1,3 years (mean±SD, range 26-30). All subjects were right-handed. The dominant eye was the right eye in 7 cases and the left eye in the other 2 cases. BCVA in logMAR was bilaterally equivalent to 0,0 corresponding to 20/20 with ETDRS; the best optical correction was -2,83±1,75 SE (mean±SD, range -1,50/-4,5) for both dominant eye and for non-dominant eye.

The analysis in the two groups of the parameters of age, refraction and visual acuity (Student-t Test) yielded the following results: no significant difference between the average age in the two groups; the groups were therefore considered homogeneous (p=0,107); refraction averages in the normal subjects and in the amblyopic subjects were quite different for both the dominant eye and for the non-dominant eye (p<0,01); amblyopic eye was slightly more hypermetropic than the dominant eye (p=0,065). This difference was not found in the control group; BCVA of the dominant eye was 0,0 logMAR in both the Study Group and in the control group. A significant difference was also present between BCVA of the non-dominant eye in the controls and in the amblyopic subjects (p<0,001).

The application of the linear regression test yielded the following results: no significant correlation was noticed between RT and age of the patients, during both monocular and binocular vision; similarly, in the amblyopic subjects, no relation between RT and strabismic deviation was present. Thus, any kind of influence of the latter on the answer speed has to be excluded. This also includes the possibility that the amount of strabismic deviation does not affect the answer speed.

The Student-t Test and the Variance Analysis Test (ANOVA) showed the following relations: in both groups, RT represented a decreasing function of the stimulus dimension, for all the procedures of presentation. This tendency was not statistically different between the two groups: ANOVA Test p=0,471. (Figs. 1, 2); in both groups, RT values deriving from the greatest stimuli were rather inferior to those measured with smaller stimuli. This was true for all the stimuli: Student "t" Test and ANOVA Test p <0,001. (Figs. 1, 2); in the Study Group the same stimulus produced longer reaction times in the amblyopic eye compared with those of the dominant eye (p<0,001), as well as those recorded during binocular vision (p<0,001); on the contrary there is no difference between the dominant eye and binocular RT, as seen in Table 1; as reported in Table 2 the same stimulus in the Control Group did not produce any difference between RT in the non-dominant eye and the dominant eye, as well as in binocular vision.

With regards to the response of the amblyopic eye, there was no relation between the visual acuity and the reaction times derived from stimuli of different dimensions (values of significance equivalent to 0.103 for the stimulus S 0.2, 0.604 for the stimulus S 0.5, 0.578 for the stimulus S 1, 0.273 for the stimulus S 2, respectively).

Discussion

The few existing studies on RT in amblyopic subjects show an increase of such times for the amblyopic eye in comparison with the non-amblyopic

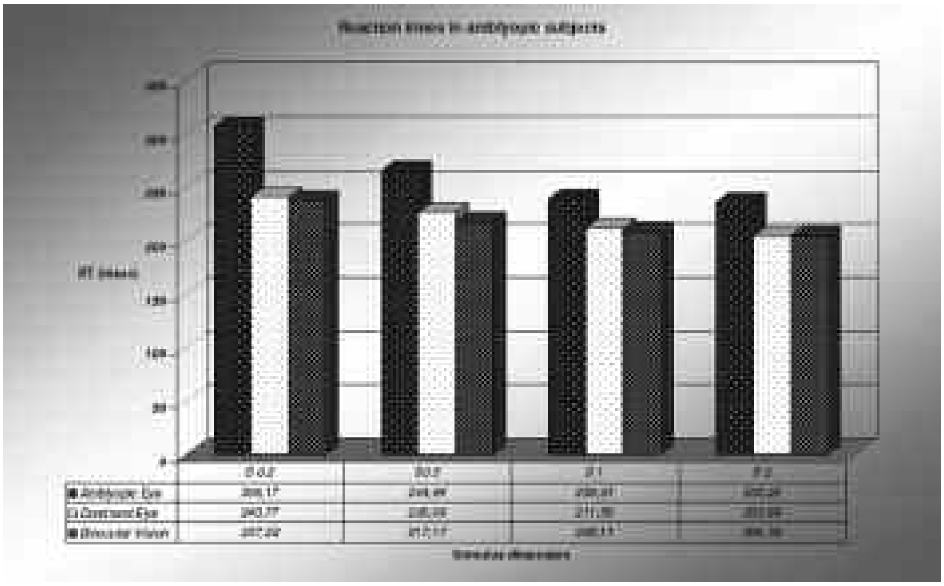

Figure 1. Reaction times in amblyopic subjects

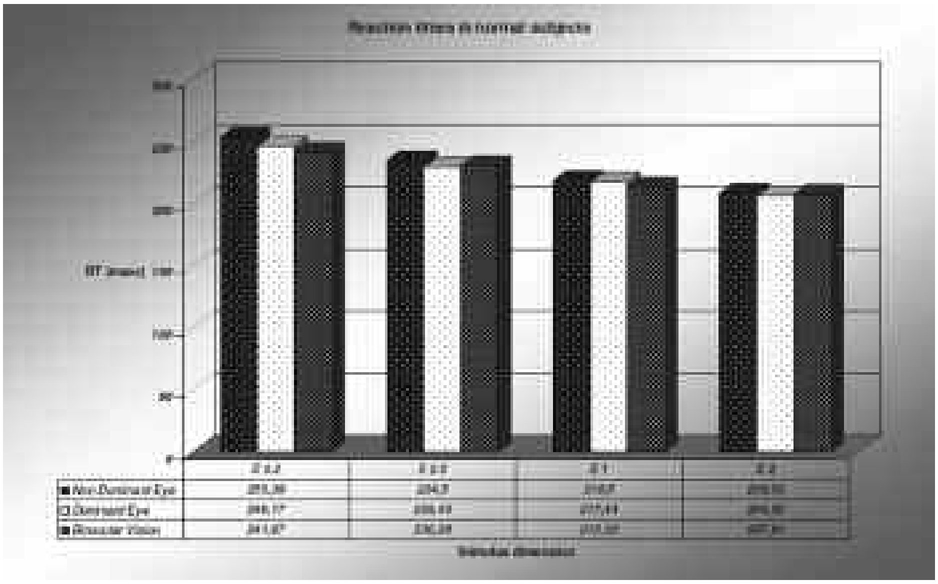

Figure 2. Reaction times in normal subjects

eye and the binocular vision (3-5). On the contrary, in normal subjects no differences in visual reaction times were found between the two eyes (3, 4). Even though a relation between visual acuity and visual reaction time in the amblyopic eye could be assumed (3), such a delay in the reaction time was stable for all the dimensional levels of the stimuli when visual stimuli corresponding to different levels of visual acuity were used (4). The two stimuli used in this study implied visual angles of 0.25° and 0.5°, corresponding to values

Table 1. Reaction Times (mean±SD) to different stimuli dimensions and different means of presentation in amblyopic subjects (Anova test)

Stimulus Dimension	RT in Amblyopic Subjects				Comparison between Binocular (BIN) and Monocular Vision (DOM-AMB)
	Dominant Eye	"p"	Amblyopic Eye	Binocular Vision	
S 0.2	240.7±22	0.00012	306.1±40	237.2±22	BIN vs DOM: "p"= 0.712 BIN vs AMB: "p"= 0.00012
S 0.5	226±20	0.00012	264.9±49	217±18	BIN vs DOM: "p"= 0.208 BIN vs AMB: "p"= 0.00014
S 1	211.5±21	0.00012	238±36	208±23	BIN vs DOM: "p"= 0.721 BIN vs AMB: "p"= 0.00013
S 2	203.8±24	0.00014	235.2±36	204.3±27	BIN vs DOM: "p"= 0.912 BIN vs AMB: "p"= 0.00014

Table 2. Reaction Times (mean±SD) to different stimuli dimensions and different means of presentation in normal subjects (Anova test)

Stimulus Dimension	RT in Normal Subjects				Comparison between Binocular (BIN) and Monocular Vision (DOM-NDOM)
Eye	Dominant Eye	"p"	Amblyopic Vision	Binocular	
S 0.2	246.7±21	0.114	253.1±27	242±18	BIN vs DOM: "p"= 0.954 BIN vs NDPM: "p"= 0.359
S 0.5	229.5±17	0.498	234.9±21	230.2±20	BIN vs DOM: "p"= 0.998 BIN vs NDPM: "p"= 0.353
S 1	217.4±16	0.816	218±17	213±17	BIN vs DOM: "p"= 0.636 BIN vs NDPM: "p"= 0.664
S 2	206.5±19	0.977	208±17	207.5±16	BIN vs DOM: "p"= 0.986 BIN vs NDPM: "p"= 0.944

of visual acuity of 20/50 and 20/100 respectively. Thus, RT were worse for the smallest stimulus than for the greatest one. Levi et al. (5) found that at all spatial frequencies and contrast values, RT in the amblyopic eye were prolonged compared to the nonamblyopic eye, especially at high spatial frequencies.

According to previous studies, we recorded a much longer reaction time in amblyopic eyes. This delay did not depend on visual acuity nor on age and strabismic deviation. The absence of relation with visual acuity could be due to the fact that the cross-eyed subjects from our study group were selected since they were able to perceive all four stimuli proposed during the tests. As we have already pointed out, the dimension of the visual stimulus was inversely related to the reaction time, in both strabismic and in normal subjects. It could therefore be assumed that, even under normal visual acuity conditions, the exact perception of the stimulus, with the consequent motorial reaction, is perceived in different ways according to the type of the proposed stimulus. However, our experimental conditions do not enable us to obtain suitable conclusions.

RT values measured during both binocular and monocular vision with the dominant eye did not show any significant difference in the study group or in the control group. This was probably due to the use of stimuli with characteristics that make them unable to reveal the effects of the binocular summation in the normal subject. This therefore jeopardizes any attempt to highlight a possible contribution of the binocular vision in the amblyopic subject with anomalous retinal correspondence. From a clinical point of view the study of the RT to visual stimuli could supply objective information on uncertain or hidden amblyopia. The limit of this measurement is the degree of compliance, which is unpredictable and probably difficult to reproduce in subjects under pre-school age: should that become possible, RT could represent an important parameter for the diagnosis of amblyopia.

Acknowledgements

The authors thank Cristiana Cantù, MD and Giuseppe Cavallero, MD, for their collaboration during patient recruitment and for statistical assistance.

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Accepted: 6th November 2007
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