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ACUTE ACQUIRED CONCOMITANT ESOTROPIA ASSOCIATED WITH MYOPIA: IS THE CONDITION RELATED ON ANY BINOCULAR FUNCTION FAILURE?

Celeste Ruatta, MD*, Costantino Schiavi, MD*

*University Eye Clinic, St. Orsola-Malpighi Teaching Hospital, Department of Experimental, Diagnostic and Specialty Medicine – DIMES, University of Bologna, Italy

Address of the corresponding author: celesteruatta@gmail.com

Abstract:

Purpose: To evaluate the sensory-motor state, accommodation, and accommodative convergence to accommodation ratio (AC/A) in a cohort of non-amblyopic myopes with acquired concomitant esotropia (Bielschowsky esotropia, BE).

Methods: Refraction, near and far deviation, fusional amplitude (FA), near point of accommodation (NPA), AC/A (gradient method), and stereopsis were measured in a cohort of 26 patients (25 phakic and 1 pseudophakic, age: 14-60 years) with BE, prospectively recruited from January to September 2019 at St. Orsola-Malpighi Hospital, Bologna, Italy. The Pearson's Correlation Coefficient was used to correlate distance with near deviation, distance with near divergence FA and angle of deviation with FA (statistical significance: p -values < 0.05).

Results: Myopia range was 0-17,5 dioptres (D) spherical equivalent (mean: 4,4D). A positive correlation resulted between distance (mean: 23,7 prism dioptres/PD, range: 4-40PD) and near (mean: 23,7PD, range: 2-45PD) deviation ($p < 0.00001$) and between distance (mean: 12,6PD, range 0-34PD) and near (mean: 17,0PD, range 3-36PD) divergence FA ($p < 0.00001$). A non-significant correlation resulted between angle of deviation and divergent FA at near (p 0.07) and distance (p 0.13) fixation. NPA was within normal limits for age. AC/C ratio range was 0-8 (mean: 3). Twenty-three patients showed randot stereopsis.

Conclusions: BE shows high variability of age of onset, degree of associated myopia, AC/A, and divergent FA. A little stronger near divergent FA can justify the better compensation at near fixation. These results show that uncorrected myopia, accommodation, and divergence paralysis do not concur to the genesis of BE.

KEYWORDS: acute acquired concomitant esotropia; distance esotropia; adult esotropia; Bielschowsky concomitant esotropia; myopia; horizontal diplopia

INTRODUCTION

Acute acquired concomitant esotropia (AACE) is a rare presentation of esotropia which occurs in children, adults and even the elderly [1]. Three main types have been defined by Burian and Miller in 1958: 1- Swan type concomitant esotropia due to the disruption of fusion precipitated by monocular occlusion or loss of vision in one eye in infants or children [2]; 2- Burian-Franceschetti type: concomitant esotropia characterized by minimal hypermetropia and diplopia, which is often associated with physical or psychological stress in teenagers and young patients; 3- Bielschowsky type: concomitant esotropia which can arise from adolescence to the elderly in myopic patients [3]. In Bielschowsky esotropia (BE), patients are myopic and exhibit a symptomatic esodeviation which is usually small at the beginning and present only at distance fixation, whereas binocular single vision for near is retained. The angle of deviation increases over time and symptoms become constant, at distance and near [4]. The origin of BE is still unclear. Bielschowsky had no doubt that the myopia in these patients played a central role in its etiology [5]. Like von Graefe, he assumed that the uncorrected myope tends to hold print excessively close to the eyes, thus resulting in an inability to maintain a balance between the converging and diverging forces of the eyes [6]. Since abduction may be slightly restricted in some cases, Burian and Miller suggested that this type had to be identified with a paralysis of divergence [3]. Other causes have been hypothesized for this condition like bilateral lateral rectus muscle weakness, convergence spasm, or accommodation disturbances without however any conclusive demonstration of a certain cause [7][8]. Since the cause, motor or sensory, of this form of concomitant strabismus is still unclear, we investigated the binocular functions, i.e., divergence and convergence fusional amplitudes (FA), stereopsis, accommodative convergence to accommodation ratio (AC/A) and near point of accommodation (NPA) in a series of patients referred to our department for BE with myopia in the last year.

MATERIALS AND METHODS

Patients who met the following criteria were included in this prospective study: (1) acquired concomitant esotropia with the presence of diplopia starting at far fixation; (2) myopic refractive error preceding the onset of the deviation; (3) age >5 years at the time of diplopia onset; (4) corrected visual acuity of better than 20/25 in both eyes; (5) normal ocular motility, i.e., concomitant esotropia with deviation in all gaze directions differing by ≤ 2 prism dioptres (PD) when primary deviations were ≤ 20 PD and by ≤ 5 PD when primary deviations were > 20 PD; specifically, patients with limitation of abduction and of elevation were excluded, since it could point

to the heavy eye syndrome with dislocation of the lateral and superior rectus muscles; (6) no cause of interruption of fusion; and (7) no history of systemic disease, head trauma, neurological pathologies, latent or manifest strabismus during infancy. Particularly, all patients must not have had early childhood esophoria or esotropia.

Twenty-six patients (14 males and 12 females) with acquired concomitant esotropia and myopia who met the inclusion criteria were prospectively recruited and assessed between January 2019 and September 2019 at the University Eye Clinic of St. Orsola-Malpighi Teaching Hospital, Bologna, Italy. The mean age of the patients at the time of inclusion in the study was 34.2 years (range, 14 - 60 years). In all of them, the esotropia had developed from 1 to 5 years before their eye examination. The delay in presentation was attributable to delay on the part of either the referring physician or the patients themselves. These patients' data are summarized in Table 1.

All patients wore full optical correction and declared to regularly wear either spectacles or contact lenses during all day. Presbyopic or pseudophakic patients wore both the for far and for near correction.

In all patients, diplopia was initially intermittent and only at distance fixation. Later, symptoms became constant and most of patients complained of diplopia also for near. Three patients have undergone refractive surgery in the past: patient n.2 and patient n.4 by photorefractive keratectomy (PRK) and patient n.15 by laser assisted in situ keratomileusis (LASIK). Patient n.13 was pseudophakic bilaterally. Patient n.21 previously underwent surgery for BE, and he suffered a recurrence of the esotropia. No patient presented any neurological pathology. Many patients had undergone brain magnetic resonance imaging which resulted normal in all of them.

The following data were collected from patients: age, gender, visual acuity, cycloplegic refractive error, angle of deviation for near and distance fixation, AC/A ratio, divergent and convergent FA, measurement of near stereoacuity with the TNO test and NPA. All measurements were performed by the same physician. Angle of strabismus was measured with the prism and cover test for near (33 centimetres) and distance (6 meters) fixation, as well as for all directions of gaze, with full refractive correction, and recorded in PD. In all measurements, an accommodative target was used. AC/A ratio was obtained measuring again the deviation at the same distance of 6 meters as before but with -1.00 D lenses added to the full refractive correction. The stimulus AC/A ratio was calculated by dividing the difference between the deviation detected with the -1 D lenses placed before the spectacles and that measured without the -1 lenses addition, by the accommodative demand of -1.00 D (far gradient method). Minus addition was limited to -1 lens since some patients were presbyopic and one pseudophakic. The normal AC/A ratio is between 3 and 5 [9]. Divergence and convergence

FA were measured at distance and at near fixation through the full optical correction with one or two Berens' horizontal prism bars, depending on the angle of deviation. In presbyopic and in pseudophakic patients the optical correction for near was used for the near FA assessment. An accommodative target was used first at distance (6 meters) and then at near (33 cm). Divergence FA measurements preceded convergence FA evaluation, as divergence is significantly reduced if assessed after convergence [7]. Starting from the base out prisms totally compensating the deviation, base out prisms of decreasing power and of increasing power were used to measure divergence and convergence FA, respectively. The fusional divergence break point was identified as the base-out or base-in prism strength at which an esotropia occurred and could not be compensated. A short time was allowed for spontaneous recovery of fusion after an esotropia occurred. Then, the prism strength was gradually increased (when base-out) or decreased (when base-in) until the patient could fuse again the target. When fusion was re-established, the power of the prism was recorded as recovery point. The fusional convergence break point was identified as the base-out prism power at which an exotropia occurred and could not be compensated. Then, the prism power was gradually decreased up to the point in which the patient could fuse again at the recovery point. Convergence and divergence break point and recovery point were confirmed by brief cover test because patients may have lacked awareness of diplopia. The real value in PD of the break point and the recovery point was calculated by subtracting the break point or the recovery point value respectively from the angle of strabismus while measuring divergence FA, and by subtracting the angle of strabismus from the break point or the recovery point value respectively while assessing convergence FA. Measurements were repeated two, three or more times in order to ascertain that the results were plausible. When two consecutive measurements gave the same result, this data was kept valid [10].

Near stereopsis was evaluated with the TNO test (Laméris Ootech B.V., Nieuwegein, the Netherlands). Stereoacuity scores were reported in seconds of arc.

The NPA was subjectively measured with the best optical correction in place. While the participants focused monocularly on the "E" one line above their near visual acuity threshold, the near Snellen E chart was gradually moved toward them in a Beren's ruler until they reported that the letter was blurry, and they were no longer able to maintain a clear image. At this point, the distance between the target and the spectacle plane was measured in centimetres. NPA was repeated twice for all patients, and the two measures were averaged.

All study participants underwent surgery which consisted of graduated unilateral or bilateral medial rectus muscle recession.

Written informed consent was obtained from all individual participants included in the study or their parents when minors. The Pearson's Correlation Coefficient was used to correlate the angle of deviation at distance fixation with the angle of deviation at near fixation, divergent FA at distance with divergent FA at near fixation and the angle of deviation with divergent FA. Since the data were normally distributed, p-values < 0.05 were considered statistically significant.

Table 1 Characteristics of patients. Abbreviations: N.: Number; M: Male; F: Female

Patient N.	Sex	Age (years)	Diplopia Onset (months)
1	M	36	24
2	M	36	18
3	M	23	12
4	F	44	24
5	F	15	24
6	M	44	48
7	M	25	36
8	F	48	28
9	F	43	48
10	F	47	12
11	M	28	60
12	F	50	48
13	M	49	36
14	F	22	48
15	F	49	12
16	M	39	12
17	F	60	36
18	F	20	36
19	M	24	24
20	F	25	12
21	M	29	12
22	M	14	48
23	F	50	24
24	M	16	60
25	M	33	48
26	M	21	12

RESULTS

The mean myopic error was -4.4 dioptres (D) spherical equivalent (SE) (range, -1.0 - -15.3D) in the right eye, while it was -4.3 D SE (range, 0 - -17.5D) in the left eye.

The mean angle of esotropia was 23.7 PD for distance fixation (range, 4 - 40 PD) and 23.7 PD for near fixation (range, 2 - 45 PD). In each patient, the angle of deviation for distance and for near fixation were nearly equivalent, differing by $\leq \pm 5$ PD. In fact, a strong statistically significant positive correlation was found between the mean angle of deviation at near and that at distance fixation (p -value < 0.00001).

As regards FA measurements, we decided to consider the break point values as the measure of FA, as they resulted more stable during repeated tests, compared to recovery point values which mostly in divergence showed a somewhat variable behaviour. At distance fixation, divergent FA ranged from 0 to 34 PD (mean, 12.6 PD) and convergent FA ranged from 0 to 45 PD (mean, 15.5 PD). At near fixation, divergent FA ranged from 3 to 36 PD (mean, 17.0 PD) and convergent FA ranged from 5 to 45 PD (mean, 18.1 PD). In 58% of the patients, the negative FA at near was higher than at distance, in 27% they were equal and in 15% of the cases they were higher at distance.

The horizontal deviation of each patient with convergent and divergent FA measured by prism bar at distance are shown in Figure 1. The horizontal deviation of each patient with convergent and divergent FA measured with the same method at near are shown in Figure 2. In only 3 out of 26 study patients the divergent FA was large enough to compensate the esodeviation at distance. In Figure 1 these patients may be identified as the patients where the down bar reaches or exceeds the 0 line, meaning that divergent FA at distance is equal or larger than esodeviation at distance. At near fixation, 13 out of 26 patients showed divergent FA large enough to compensate their esodeviation. In Figure 2, these patients can be identified as the patients where the down bar reaches or exceeds the 0 line, meaning that divergent FA at near is equal or larger than the esodeviation at near.

A strong statistically significant positive correlation was found between divergent FA at distance and divergent FA at near fixation (p -value < 0.00001).

A statistically non-significant correlation was found between the angle of deviation and the divergent FA at near (p -value 0.07) and at distance fixation (p -value 0.13).

The overall mean AC/A ratio was 3 (range, 0 - 8). For patients aged 14 to 24 years old, the mean AC/A ratio was 3.62, for patients aged 25 to 44 years old, it was 3.18 and for patients aged 45 to 60 years old, it was 2.14.

Stereopsis, evaluated by TNO test, was 480 arc seconds in 5 patients, 240 arc seconds in 8 patient, 1980 arc seconds in 10 patients, and absent in 3 patients.

NPA was normal in all phakic patients, according to patient age.

These patients' data are summarized in Table 2.

Anterior segment examination and fundoscopy were normal except for mild myopic retinal changes seen in some patients. All patients underwent surgery. After the operation, all were found to be orthophoric or minimally esophoric.

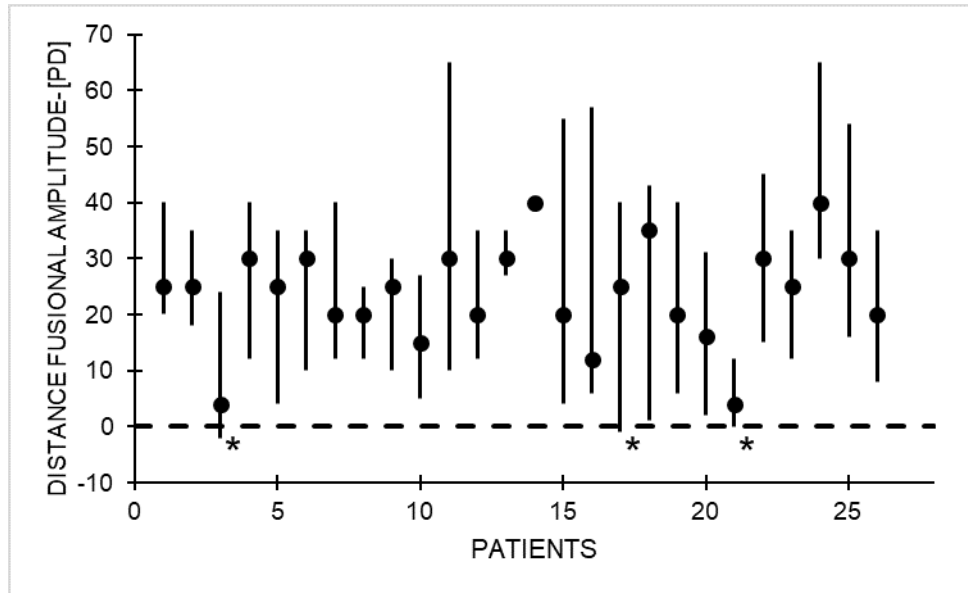


Fig. 1 Horizontal deviation in prism dioptres (PD) indicated with a black spot, with the horizontal fusional amplitude in PD at distance (6 m) in the patients enrolled in the study. The upward bars, starting from the angle of the horizontal deviation, represent the convergent fusional amplitude. The downward bars, starting from the angle of deviation, represent the divergent fusional amplitude. Star sign indicates patients whose downward bar reaches or exceeds the 0 line.

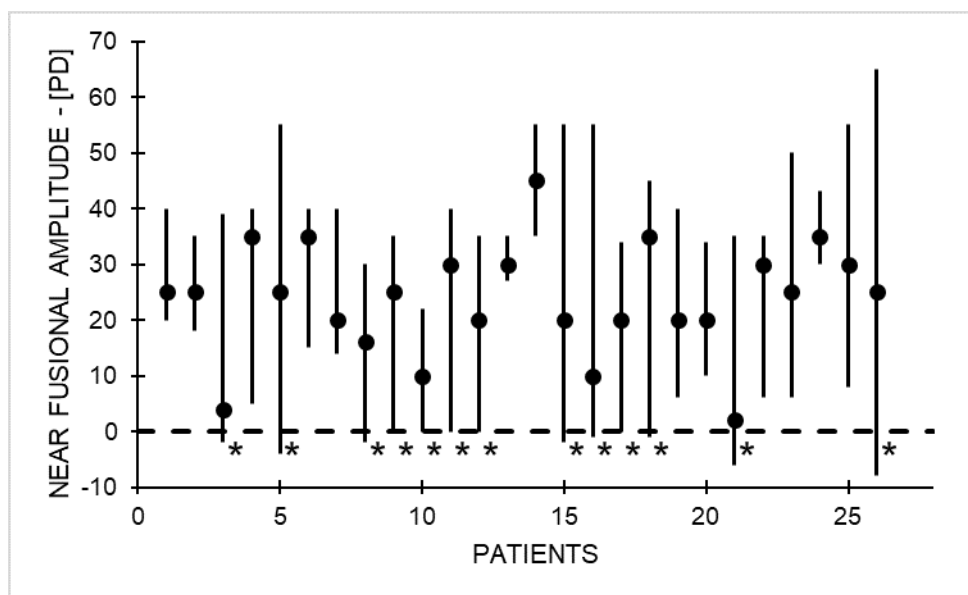


Fig. 2 Horizontal deviation in prism dioptres (PD) indicated with a black spot with the horizontal fusional amplitude in PD at near (33 cm) in the patients enrolled in the study. The upward bars, starting from the angle of the horizontal deviation, represent the convergent fusional amplitude. The downward bars, starting from the angle of deviation, represent the divergent fusional amplitude. Star sign indicates patients whose downward bar reaches or exceeds the 0 line.

Table 2 Clinical characteristics of patients. Abbreviations: N.: Number; D: Dioptres; SE: Spherical Equivalent; RE: Right Eye; LE: Left Eye; PD: Prism Dioptres; FA: Fusional Amplitude; Conv.: Convergence; Div.: Divergence; Cm: Centimetres; "': Arc seconds

PATIENT N.	Myopia (D/SE) RE	Myopia (D/SE) LE	Esodeviation [PD]		Distance FA [PD]		Near FA [PD]		AC/A	NPA [cm]	Stereopsis ["]
			Distance	Near	Conv.	Div.	Conv.	Div.			
1	-2,25	-2,25	25	25	15	5	15	5	0	15	1980
2	-2,5	-3,5	25	25	10	7	10	7	0	15	240
3	-3	-3	4	4	20	6	35	6	0	10	480
4	-2,75	-2,5	30	35	10	18	5	30	5	25	480
5	-3,25	-4,25	25	25	10	21	30	29	0	5	1980
6	-5	-5	30	35	5	20	5	20	5	20	1980
7	-4	-4	20	20	20	8	20	6	1	10	480
8	-1,25	-1,75	20	16	5	8	14	18	0	35	240
9	-6,25	-3,75	25	25	5	15	10	25	5	25	240
10	-4,25	-3,75	15	10	12	10	12	10	2	60	240
11	-2,5	-2,75	30	30	35	20	10	30	3	15	480
12	-15,25	-17,5	20	20	15	8	15	20	0	35	absent
13	-1	-1	30	30	5	3	5	3	0	100	absent
14	-5,75	-4,5	40	45	0	0	10	10	1	10	240
15	-3,75	-5,75	20	20	35	16	35	22	5	50	1980
16	-4,5	-3,75	12	10	45	6	45	11	6	20	1980
17	-4,5	-5	25	20	15	26	14	20	5	100	240
18	-4	-3,75	35	35	8	34	10	36	8	10	1980
19	-7,25	-6,25	20	20	20	14	20	14	5	10	1980
20	-2,25	-2,25	16	20	15	14	14	10	1	8	240
21	-5,25	-3,75	4	2	8	4	33	8	4	7	240
22	-3,75	-3,75	30	30	15	15	5	24	5	8	1980
23	-4	-4	25	25	10	13	25	19	3	100	1980
24	-6,75	-6,5	40	35	25	10	8	5	5	10	absent
25	-2	0	30	30	24	14	25	22	5	12	1980
26	-6,5	-6,5	20	25	15	12	40	33	5	10	480

DISCUSSION

To the best of the authors' knowledge, this study is one of the first to report the features of BE in a large cohort of patients.

We observed a high variability of the onset age, with the youngest patient being 14 and the oldest 60 years old, as well as of the degree of myopia. One patient showed a monocular myopia and to our knowledge, this is the first case to be described of a BE associated to a monocular myopia. Another patient showed high myopia (around 15/17 D), according to other studies that reported the occurrence of this form of strabismus even in high entities of myopia [11][6]. The clinical impression is that of an increasing incidence of this type of acquired strabismus that coincides with the spread of myopia and an ever-growing involvement in indoor activities at every age all over the world. Indeed, BE is thought to be related to excessive near work holding printed materials excessively close to the eyes [5]. In this study, all our patients referred to spend a prolonged period performing tasks requiring near vision, so we agree with other Authors [11] that prolonged near work can be a risk factor for the development of the deviation [11][12].

One of the main characteristics observed in our patients was an intermittent onset of diplopia rather than an acute one: no patient could remember the exact moment in which the symptoms started, since in the early stages they just suffered isolated episodes of diplopia. Particularly, symptoms seem to arise while looking far away, driving or watching the TV in the evening when the visual field width is reduced, and fatigue begins to be felt. Therefore, we suggest that this form of strabismus should be more properly named "concomitant esotropia" rather than "acute concomitant esotropia", as it has been called until now.

BE may be confused with decompensation of an esophoria or of an accommodative esotropia which may simulate it when normosensorial patients, usually teenagers who are becoming myopic, start to wear minus lenses [13]. In these cases, however, esotropia and diplopia start at near fixation while typically in Bielschowsky esotropia the deviation and symptoms start at distance. This sign, together with patient's history attesting that a latent or compensated deviation precedes in time the onset of myopia, is the main distinctive factor between the two conditions. In BE patients instead there is not a history of strabismus during infancy, and the myopia precedes in time the onset of the strabismus.

BE shows a characteristic onset of symptoms at distance fixation. Since angles of deviation for distance and for near were nearly equivalent in our patients, compensation for the deviation at near cannot be explained by a lesser amount of deviation. Therefore, we investigated whether there may be a decreased ability to diverge at distance by analyzing motor fusion. We noticed that divergent FA was present with values similar to those of normal subjects in all patients but for the majority of them it was not strong enough to correct the esodeviation at distance fixation. On the other hand, in many patients divergent FA was sufficient to compensate the esodeviation at near fixation. The better compensation of the deviation at near seems to be related to the wider divergent motor fusion at near with respect to that at distance fixation, since the deviation is the same at far and near. This can justify why these patients are bothered by diplopia mostly at far fixation rather than at near.

The angle of deviation resulted not to be correlated with divergent FA. This means that in BE, unlike what happens in other forms of strabismus like intermittent exotropia [14], FA do not follow the angle of deviation, somehow adapting to it.

We noticed that while the deviation seems apparently to be of small entity and only for distance fixation, it often proves to be of greater amplitude when measured with the cover test. Performing a very dissociating cover test in these patients is important in order to avoid underestimations of the amount of the deviation and consequently surgical under corrections. A very dissociating cover test serves in these patients to unmask the deviation, mostly at near fixation, where it is often tenaciously compensated.

In most of our patients, a normal stereopsis was present before surgery, through prismatic correction of the angle of deviation. The postoperative orthophoric position and normal fusional capacity were re-established in all patients who received unilateral and bilateral medial rectus recession. This confirms Spierer's theory which states that when normally developed binocular vision is disrupted after the onset of strabismus, binocular capacity is potentially preserved and can be later regained after the strabismus is surgically corrected [4].

This type of strabismus has been recognised for years, though its etiology is still unclear. Bielschowsky claimed that uncorrected myopia played an important role in its origin [5]. In the present study, all patients were myopic and all wore spectacles at presentation, leading us to conclude that uncorrected myopia could not be considered among the causes of the BE, according to other reports found in literature[15].

It was then speculated that a cause might be an excess of accommodation and therefore of convergence [7][8].

In our study we showed that this esotropia may develop even in patients in which accommodation is absent, as in pseudophakic or presbyopic patients. Moreover, we studied some accommodative functions, as the NPA and the AC/A ratio, and they resulted to be within normal limits on average. NPA was normal in all phakic patients,

according to patient age. AC/A ratio was normal in all but two patients (n.16 and n.18). In our patients, the AC/A ratio slightly decreased with age. This effect is inconsistent with some reports which described a slight AC/A increase with age up to 45 years [16][17]. Conversely, the AC/A ratio decrease found in our study is consistent with the results of another study, which registered no systematic age effect for patients up to 45 years old and a slight AC/A decrease in older patients[18].

These findings, together with the occurrence of this strabismus in young, adult, presbyopic and pseudophakic patients, clearly indicates that the mechanism of accommodation can be excluded from the causes.

Since the divergence motor fusion resulted to be within normal limits on average, a divergence paralysis in this form of strabismus may be excluded, confirming other results found in literature [15]. Moreover, divergence paralysis shows a sudden onset after head trauma or other neurological problems, whereas BE arises not acutely but intermittently and progressively, without any apparent cause.

None of the patients had an obvious underlying neurological disease.

Concluding, BE shows some peculiar characteristics: the gradual, not striking onset of the symptoms at distance; the high variability of age of onset and degree of myopia associated; the difficulties experienced while tempting to measure the angle of strabismus in these patients in which a very dissociating cover test is needed; the better compensation of the strabismus at near in the presence of almost equal angles of deviation, which seems to be due to the higher divergent fusional amplitudes at near than at distance; the occurrence of this form of concomitant strabismus also in ex-myopes, i.e., patients that underwent refractive or cataract surgery, and also in presbyopic myopes. The etiology of this form of strabismus remains unclear. In our study most of the patients usually wore spectacles correcting their myopia and they had normal motor fusion, normal accommodative functions and normal binocular vision potential. Therefore, we do not deem uncorrected myopia, divergence paralysis or accommodative element as the genesis of Bielschowsky concomitant esotropia.

Compliance with Ethical Standards:

Funding: The authors received no funding for this work.

Conflicts of interest: All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in

speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements) or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethics approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the St. Orsola-Malpighi Teaching Hospital of Bologna, Italy, and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

This article does not contain any studies with animals performed by any of the authors.

Informed consent: Written informed consent was obtained from all individual participants included in the study or their parents when minors.

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