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Effect of prolonged monocular occlusion on latent nystagmus ◇

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ABSTRACT. The authors recorded nystagmus during seeing with one eye in eight patients with latent nystagmus (LN) before and after two or three days of prolonged occlusion of the better eye (POBE). Before POBE, the slow-phase speed of the nystagmus (SPS) was usually higher when the better eye was covered. After POBE, the SPS during cover of the better eye had decreased and the SPS during cover of the poorer eye had increased (please note the time difference between 'prolonged occlusion' and 'cover'). However, the sum of the two speeds (absolute values, for they were opposite in direction) remained the same in all cases. This indicates that the principal component of the LN, the difference between LN with right- and LN with left-eye cover, remained the same, but a drift towards the poorer eye had been added that decreased the SPS during cover of the better eye and increased the SPS during cover of the poorer eye. In three patients who had oscillopsia during POBE, the oscillopsia gradually decreased over days during POBE, indicating that the drift changes slowly, over a period of days. As regards occlusion therapy in children with amblyopia and latent nystagmus, based on these findings, it seems advisable to occlude the better eye during days per week, rather than during hours per day: Then there is more time for the nystagmus to decrease, so that amblyopia therapy can be more effective.

Key words: eye movements; latent nystagmus; strabismus; amblyopia; occlusion therapy

INTRODUCTION

The infantile or congenital strabismus syndrome consists of strabismus acquired before the age of six months, with dissociated vertical deviation or latent nystagmus (LN), or with both. By definition, LN is manifest only when either eye is covered. When neither eye is covered, no nystagmus is present. When the left eye is covered, both eyes move slowly to the left, and this slow eye movement is interrupted by fast eye movements to the right. When the right eye is covered, both eyes move slowly to the right, and this slow eye movement is interrupted by fast eye movements to the left.

Curiously enough, it is sufficient for the patient to believe that he is seeing with either eye, even when the eyes are closed[2], when the patient,

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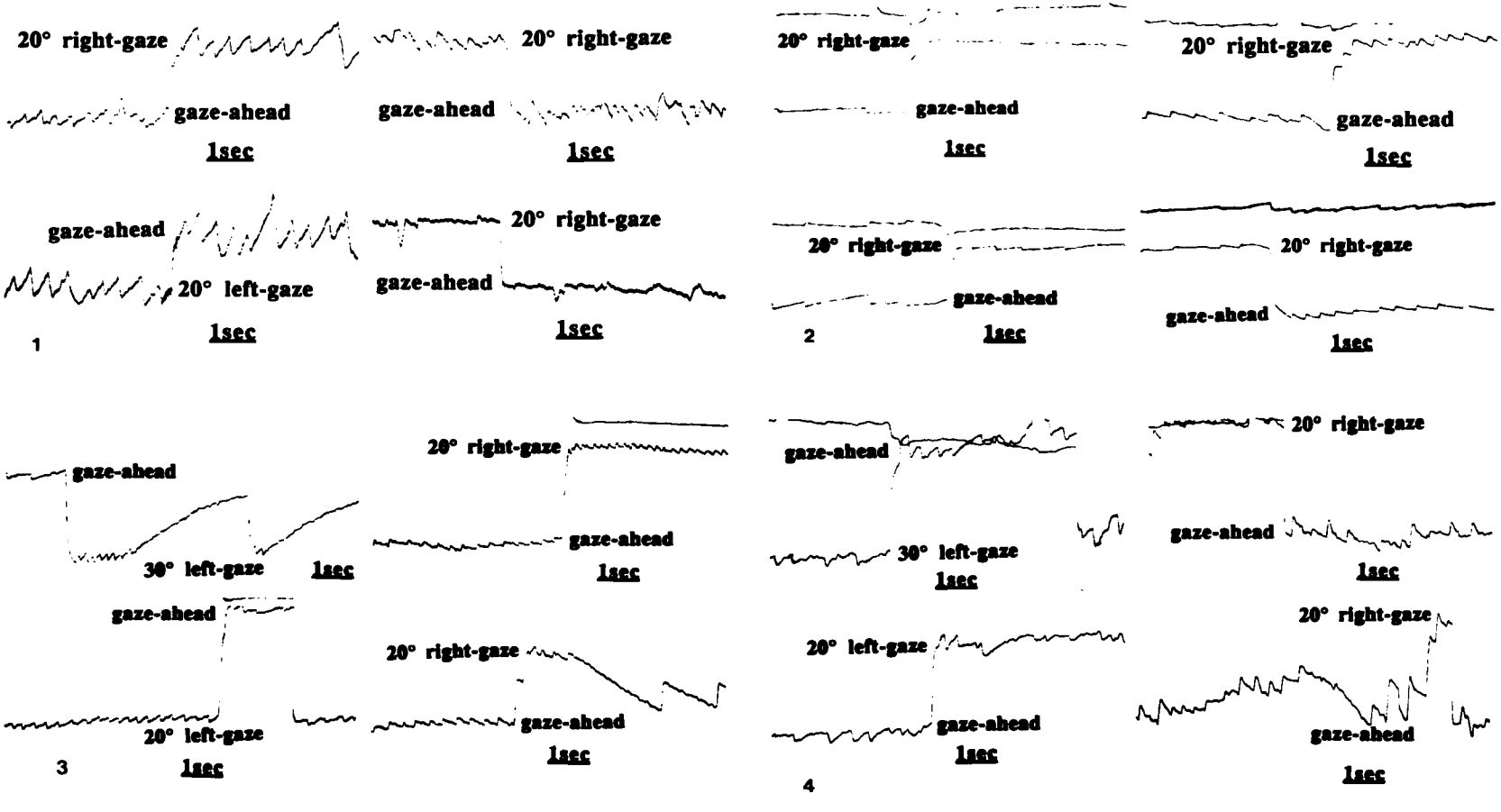

Figs. 1-8. Latent nystagmus during left- and right-eye cover, before and after POBE. Figure numbers correspond to case numbers. Of each case, four recordings are depicted: right-eye cover before POBE (top left), left-eye cover before POBE (top right), right-eye cover after POBE (bottom left) and left-eye cover after POBE (bottom right). In Patients 3, 4, 5 and 6 the right eye was subjected to prolonged occlusion; in Patients 1, 2, 7 and 8 it was the left eye. Horizontal eye movements, of both eyes simultaneously, were recorded with two electrodes placed temporally of both eyes on the skin. Abscissa: time, bar equals

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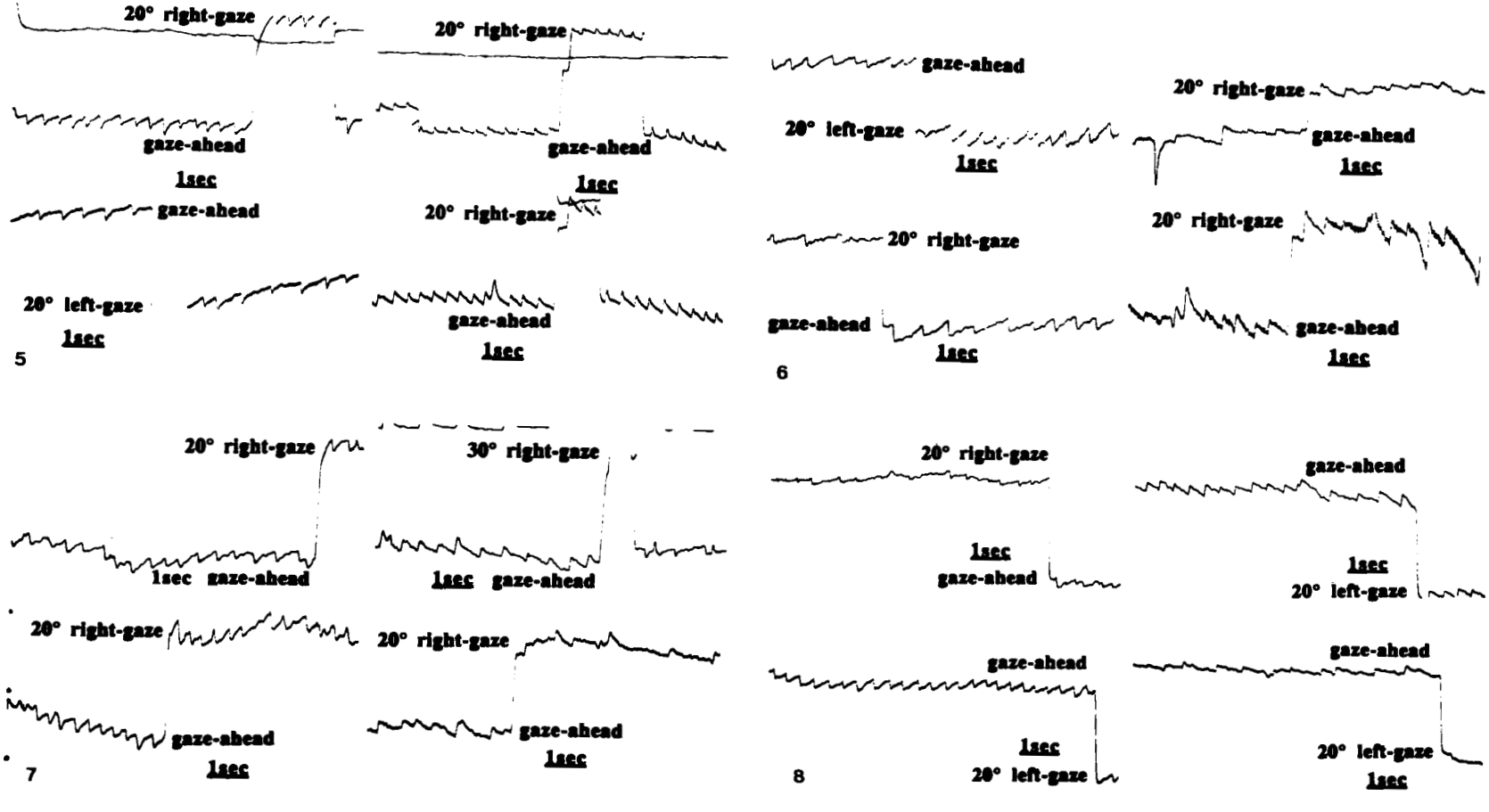

1 second. Ordinate: eye position, up is right gaze, down is left gaze. To facilitate scale reading, in each recording a part with a gaze shift of 20 degrees is included: The labels 'gaze-ahead' and '20-deg right gaze' refer to the part of the recording immediately left or right of the label. Note the increases of the SPS during CPE and decreases of the SPS during CBE after POBE.

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unknowingly, actually sees with the other eye[3,4], and even when the eye has been enucleated[5,6]. If the amounts of light entering either eye differ, this by itself may be sufficient to render the LN manifest[7].

The cause of LN has remained enigmatic. Recent studies have shown that the monocular optokinetic reflex is brisker for objects moving nasally before either eye, as opposed to that for objects moving temporally before either eye, both in children under four months of age and in patients with LN. In lower mammals it has been demonstrated that the optokinetic reflex for objects moving nasally in front of either eye is mediated by a pathway between either eye and the contralateral nucleus of the optic tract. It is thought that, in higher mammals, cortical pathways take over the optokinetic reflex during development, and this takeover does not occur if binocular vision does not develop. This would explain the increased gain of the monocular optokinetic reflex for objects moving in the nasal direction in LN[8-11].

The magnitude of LN also depends on the direction of gaze[7,12]. If the seeing eye adducts, the nystagmus decreases, and if the seeing eye abducts, the nystagmus increases. This gaze-dependent component is probably Alexander's Law ('the magnitude of a nystagmus increases when the patient looks into the direction of the fast phases'), applied to latent nystagmus. The reason for nystagmus increasing when the patient looks into the direction of the fast phases and decreasing when the patient looks into the direction of the slow phases, is most likely a drift towards the primary position (in neurophysiologic terms: a 'leaky' neural integrator function in the brainstem) similar to that seen in gaze-evoked nystagmus[13]. As in gaze-evoked nystagmus, latent nystagmus can hence have an exponential waveform, with deceleration during the slow phase. The patient with LN benefits from the leaky neural integrator by preferentially using that direction of gaze where the SPS is decreased.

Finally, in cases of amblyopia, LN is often larger and faster during cover of the better eye (CBE) as compared to that during cover of the poorer eye (CPE). It has remained unclear what causes this asymmetry between LN during CBE and LN during CPE, nor has it been studied whether or not this asymmetry varies. It is interesting to know whether and how fast the asymmetry varies, in the light of the controversy among ophthalmologists and orthoptists on whether children with LN and amblyopia should be treated with occlusion therapy or not. Many orthoptists hesitate to patch the better eye because then the LN becomes manifest, causing blurred vision. They consider atropinization and penelization to be the treatment of choice. However, von Noorden *et al.*[14] have demonstrated that occlusion therapy is feasible and effective in cases of amblyopia with latent nystagmus. We investigated the variability over time of this third component of LN by recording eye movements in eight patients with LN before and after two to three days of occlusion of the better eye (POBE) (please note the time difference between 'cover' and 'prolonged occlusion'). In short, we found that the SPS of the LN during CBE decreased and the SPS of the LN during CPE increased. However, the sum of the two speeds (absolute values, for they were opposite in direction) remained the same in all cases. This change took place very slowly, over a period of days, unlike the rapid changes of LN that take place when one or the other eye is covered or when the seeing eye abducts.

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METHODS

The patients were recruited from the strabismus outpatient department. Patients were selected on their ability to cooperate and the magnitude of the LN. Eye movements were recorded with ENG (Tönnies DC amplifier). Horizontal eye movements, of both eyes simultaneously, were recorded with two electrodes (Beckmann Instruments) placed temporally of both eyes on the skin. (Note that possible minor differences in movement of the two eyes were not registered using this method, preference being given to easier recording). Vertical eye movements were measured from one eye only, two electrodes being placed above and below one eye. The recording of vertical eye movements in these patients served mainly to register lid blinks and thus identify artifacts. All electrodes were fixed to the skin at least half an hour before registering eye movements to reduce skin resistance.

LN was recorded during binocular, during CBE and during CPE. The subjects were instructed to look at a dimly illuminated, 1-cm diameter, round fixation target in a screen approximately 1 meter in front of them. In addition, LN was recorded during 20 and 30 degrees eccentric gaze and optokinetic nystagmus was recorded, these recordings not being the subject of this paper. During the recording sessions, the room was almost dark. The recordings were recorded on paper (8-channel Siemens x-t recorder, 12 mm/s).

After the first recording session, the better eye of the patients was patched and the patients were instructed to leave the patch in place until the

TABLE 1. Essential data of the patients

Patient 1 was a 14-year-old male with a small right exotropia, dissociated vertical deviation (3-degree right hypertropia and 17-degree right hypertropia on right and left fixation). Previous 7-mm recession of the right superior rectus. Visual acuity (OD/OS): 0.4/0.4 but 1.0 binocularly, after prolonged occlusion of the left eye: 0.6/0.3. Bagolini striated glasses positive at near-fixation, diplopia at distance-fixation. Oscillopsia complaints decreased after one day of prolonged occlusion and were almost gone after two days.

Patient 2 was a 33-year-old male with 16 diopters of myopia of both eyes, a right 26-degree convergent squint and right amblyopia. Visual acuity: 0.05/0.6 with contact lenses.

Patient 3 was a 39-year-old male with a 35-degree left esotropia and an untreated left amblyopia. Visual acuity: 1.2/0.9.

Patient 4 was a six-year-old male with esophoria and a dissociated vertical deviation. Bagolini striated glasses positive. Visual acuity: 0.83/0.55.

Patient 5 was a 39-year-old female with a dissociated vertical deviation, five diopters of myopia and two diopters of astigmatism in both eyes. Visual acuity: 0.4/0.3, after prolonged occlusion of the right eye: 0.3/0.4. Oscillopsia complaints during occlusion of the right eye: The first day she went to bed, the second day the image shaked like in 'those 3-dimensional images for children that move if you tilt them', the third day the oscillopsia had disappeared.

Patient 6 was a 16-year-old female, left infantile esotropia, large dissociated vertical deviation, V-pattern, amblyopia treatment started when she was one year old. 7/7-mm recess-resect surgery for esotropia OS was done 12 years previously, an 8-mm left superior rectus recession and a 5-mm left medial rectus anteroposition were done four years previously. Visual acuity: OD: 0.4, OS: 0.1, after prolonged occlusion of the right eye: 0.4/0.4.

Patient 7 was a 15-year-old female, dissociated vertical deviation, right esotropia and right amblyopia. Visual acuity: 0.5/0.8, after prolonged occlusion of the left eye: 0.6/0.8. Five diopters of myopia and 2.5 diopters of astigmatism. 6/6 mm recess-resect surgery for esotropia OD had been performed one year previously. No oscillopsia occurred during prolonged occlusion but on taking off the patch, vertigo was experienced by the patient.

Patient 8 was a 15-year-old female with a right exotropia since age four months, dissociated vertical deviation, a right amblyopia and 3.5 diopters of myopia. Two exotropia operations and myotomies of both inferior obliques were done 12 years previously. Visual acuity: 0.5/0.8, not better after prolonged occlusion. On taking off the patch after two days, oscillopsia and vertigo were experienced by the patient.

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TABLE 2. The magnitude of the SPS during seeing with both eyes, with the right eye or with the left eye are given below for all patients. The SPS is expressed in degrees per second. The SPS was measured in each trace of the recorded nystagmus by measurement, by hand, of the angle between slow-phase recording and abscissa, the tangent of this angle being proportional to the SPS (the abscissa representing time, the ordinate representing eye position). Each time, the angles of five to ten slow phases were measured and averaged. When any uncertainty arose about the magnitude of the SPS, or when the SPSs were widely different, this is indicated in the table by 'err'. Before POBE, the SPS was higher during CBE. Note that after POBE, the SPS during CBE decreased and the SPS during CPE increased. The sum of the two (absolute values, for they were opposite in direction), however, remained the same in all cases

Slow-phase speed (+ = eye movement to the right): *Patient:*	1	2	3	4	5	6	7	8
no eye covered:	0.0	+1.38	−1.31	0.0	0.0	0.0	+1.63err	0.0
left eye covered:	−12.04	−3.36	−1.33	−6.05	−4.37	−3.46	−4.58err	−4.87
right eye covered:	+8.42	+0.52	+2.45	+6.30	+4.25	+11.00	+6.18	+2.79
After 2-3 days of occlusion of the better eye (right eye in Patients 3, 4, 5 and 6, left eye in others):								
no eyes covered:	0.0	0.0	+1.44	0.0	0.0	−6.57err	+4.48	0.0
left eye covered:	−1.23	−2.51	−3.19	−10.59	−5.18	−10.80	−3.10err	−1.05
right eye covered:	+20.65	+1.88	+1.44	+3.05	+2.18	+3.52	+9.23	+5.22

second recording, two or three days later. All patients, or their parents, gave oral informed consent.

The SPS was measured in each trace of the recorded nystagmus by measurement, by hand, of the angle between slow-phase recording and abscissa, the tangent of this angle being proportional to the SPS (the abscissa representing time, the ordinate representing eye position). In each determination of the SPS, the SPSs of between five and ten slow phases were measured and averaged. When the slow phase had an exponential waveform, with deceleration during the slow phase (caused by the gaze-direction dependent component as described above) the tangent to the curve at the middle of the slow phase was taken as slow-phase speed. When the measurements were variable, or when the SPS varied considerably during one slow phase, the nystagmus was considered to be erratic (designated as such in the tables).

RESULTS

Essential patient data are given in Table 1. Figs. 1-8 (numbers correspond to case numbers) and Table 2 show that before POBE the SPS was higher during CBE than during CPE, except in cases where the visual acuity of the two eyes did not differ. After POBE the SPS during CBE had decreased and the SPS during CPE had increased. However, the sum of the two (absolute values, for they were in opposite directions), remained approximately constant in all cases. For instance, in Case 1 the SPS was −12.04 degrees/s during cover of the left eye (minus denotes leftward eye movement) and +8.42 degrees/s during cover of the right eye. After two days of prolonged occlusion of the left eye, these speeds had changed to −1.23 and +20.65 degrees/s, respectively. The nystagmus with both eyes open (designated 'manifest latent nystagmus', MLN, when occurring) did not show such a consistent change to POBE: In Cases 1, 4, 5 and 8, the MLN was zero before and zero after occlusion for two days. In Case 3, before POBE the small MLN equaled the LN during CPE; after POBE, it equaled the LN during CBE (also small). Only Cases 6 and 7 had a minor MLN that was the approximate average of that during CBE and

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that during CPE. After POBE, this changed in parallel with LN during CBE and that during CPE.

The results were less consistent for OKN gain changes (not reported in detail), although the tendencies were the same. In addition, the gaze-dependent component could not be delineated as clearly as had been expected. Oscillopsia complaints disappeared gradually during the occlusion. Patient 1 had oscillopsia only for one day. Patient 5 was occluded for three days; she told us that the oscillopsia had been unbearable the first day (she went to bed), had improved the following day, and had disappeared the third day.

Visual acuity improved only slightly in all cases after POBE, never more than one line on the Snellen chart.

DISCUSSION

When the better eye is patched in children with amblyopia and latent nystagmus, the LN becomes manifest, causing blurred vision. Under these conditions, the amblyopia treatment will be less effective. Hence atropinization and penelization are preferred to occlusion by many orthoptists and ophthalmologists. On the other hand, von Noorden *et al.*[14] have demonstrated that occlusion therapy is very effective in cases with amblyopia and latent nystagmus.

This study demonstrates that the length of the occlusion period, whether minutes, hours or days, is a very important variable in this matter. During prolonged occlusion of the better eye, the principal component of the latent nystagmus, the difference between the nystagmus during right-eye and that during left-eye cover or, in other words the sum of the SPS during CBE and the SPS during CPE (absolute values, for they were opposite in direction), remained the same, but a drift was added that decreased the SPS during cover of the better eye and increased the SPS during cover of the poorer eye.

This compensatory drift antagonized the LN made manifest by prolonged occlusion. The finding was not limited to adults or adolescents: During preparation of the manuscript, a nearly three-year-old girl was examined, and although only a few artifact-free recordings were obtained in approximate gaze-ahead, the increase of the SPS during CPE, and the decrease of the SPS during CBE were evident.

As stated above, in cases of amblyopia, LN is often larger and faster during CBE as compared to that during CPE. It is possible that this difference between LN during CBE and LN during CPE is also caused by this compensatory drift.

Is the compensatory drift (in neurophysiologic terms: a slow-phase velocity bias of the neural integrator) generated by means of visual or by vestibular information? Both mechanisms may be operative.

An acquired peripheral vestibular nystagmus caused by a unilateral labyrinthal defect decreases and disappears very rapidly, over a period of days. Here, the question is the same: is the nystagmus reduced by means of visual or by vestibular information? When cats are kept in the dark after a unilateral labyrinthectomy, the speed of the resulting vestibular nystagmus is reduced after a few days to approximately 1% of the initial SPS value (D. A. Robinson, personal communication). This reduction could be caused by modulation of the vestibulo-ocular reflex by neck afferents: these afferents register that the neck does not rotate in accordance to the vestibular nystagmus. When the cats are subsequently kept in a normally lit environment, the remaining 1% of the initial SPS of the vestibular nystagmus also disappears. The latter has been attributed to the flocculus that can modify the vestibulo-ocular

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reflex by employing visual information about the movement of images over the retina (retinal slip). Interestingly, the slow-phase velocity bias of the neural integrator becomes manifest if the second labyrinth is also removed: although both labyrinths are now lacking, a nystagmus occurs, in the direction opposite to that of the first nystagmus. Clinically this is known as Bechterew's nystagmus.

The possibility that the flocculus generates the slow-phase velocity bias by means of visual information seems attractive in our case, because it could also explain why the LN is stronger during CBE than during CPE, in cases where amblyopia is present.

As the compensatory drift changes slowly over a period of days, it seems advisable to occlude the better eye in children with amblyopia and LN during days per week, and not during hours per day: The nystagmus that becomes manifest by occluding one eye will have more time to decrease if occlusion is maintained over one day or more, and it seems likely that amblyopia treatment is more effective when retinal slip is small.

It must be noted that we found only minor improvements in visual acuity after prolonged occlusion, caused by the decrease of the nystagmus. It was never more than one line on the Snellen chart. This small increase of visual acuity caused by decrease of the nystagmus should not be confused with increase of visual acuity in the treatment of amblyopia.

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