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Optokinetic response in patients with vestibular areflexia

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Abstract. Optokinetic nystagmus (OKN) responses (stimuli 40°/s and 60°/s) were evaluated in 121 patients with vestibular areflexia (VA) and were compared with a control group of 99 control subjects matched by age. The mean response levels were significantly higher in the VA group than in the control group: 1.7°/s at 40°/s stimulation, and 4.4°/s at 60°/s. The VA group showed a significantly wider scattering and greater variances and, as a group, they exhibited higher OKN gains than the control subjects. We suggest that the higher gain of OKN responses in VA patients can be attributed to an increased efficiency in signal processing by the cortical optokinetic system. This enhancement may be similar to the enhancement which, in healthy subjects, is produced by "optokinetic training".

Keywords: Cortical optokinetic nystagmus, optokinetic training, vestibulo-ocular reflex

1. Introduction

In primates, after total loss of the peripheral labyrinthine function, optokinetic after-nystagmus is completely abolished [3,7,12,20,31,35,38,39] and, according to several reports, the level of the optokinetic nystagmus (OKN) response is decreased [3,6,38,39]. In a previous report on 27 patients with vestibular areflexia (VA) however, we described that the OKN gain (in humans) was significantly higher [18]. At 60°/s stimulation, the OKN gain increased significantly with patients' age, which is a finding that we did not understand. We stipulated the fact that the patients showed a bimodal age distribution, which might have caused some disadvantage in the statistical analyses. After having written this report, we established a control group with a suitable age distribution ($n = 99$, see below) and we examined many more VA patients, partly in the context of ongoing research projects that focused on hereditary vestibulo-cochlear hearing impairment [31–34], see for review [16] and cochlear implantation [14]. Having recruited a large group of VA patients ($n = 121$) of various ages, we decided to restudy the issue of whether the OKN gain is lower in VA patients, as compared to subjects with a normal vestibulo-ocular reflex (VOR), and whether the relation with age is relevant.

2. Methods

2.1. Patients

Our study population consisted of 121 patients with vestibular areflexia (VA) due to a diversity of causes (Table 1) and 99 control subjects. The diagnosis of vestibular areflexia was based on a lack of nystagmic responses to velocity steps of 90–250°/s (in the dark, with the eyes open); the chair was stopped at a deceleration of 500°/s^2. In the group of VA patients, 15 had (close to) normal bilateral hearing and had the following diagnoses: 3 congenital vestibular areflexia, 1 meningitis, 1 viral infection, 1 bilateral vestibular neuronitis, 3 ototoxicity (2 gentamycin, 1 streptomycin), 1 unspecified

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Table 1
Aetiology in 121 patients with vestibular areflexia

Hereditary	
Autosomal dominant late-onset progressive vestibulo-cochlear dysfunction [31,33,34]	9
Autosomal recessive congenital vestibular areflexia [32]	3
Autosomal recessive hearing impairment [14,15]	2
Otosclerosis [14]	1
Stapes gusher syndrome	1
Klippel-Feil syndrome	1
Beckwith-Wiedemann syndrome (with wide vestibular aqueduct)	1
Unspecified	7
Total	25
Acquired	
Kernicterus	1
Meningitis [14,15,17]	25
Encephalitis (echovirus)	1
Congenital cytomegalovirus infection [13]	1
Viral infection, unspecified	3
Bilateral vestibular neuronitis	2
Paratyphoid fever [17]	1
Whooping cough	1
Otogenic infection	6
Ototoxicity (gentamycin, streptomycin)	6
Trauma to base of skull [14]	6
Cogan's syndrome	5
Polyneuropathy	2
Bilateral Ménière's disease	2
Bilateral vestibular schwannoma	1
Neurological disorder, unspecified	1
Early childhood hearing impairment or deafness of unknown cause	12
Unknown cause	20
Total	96

neurological disorder and 5 unknown. Patients with a history of possible neurological complaints, or patients who had signs or symptoms of central nervous system involvement, were examined by a trained neurologist (WV). A number of 42 VA patients had bilateral complete deafness. All the other VA patients had a moderate to severe hearing impairment, either unilaterally or bilaterally, and/or were completely deaf in one ear. Only patients with a probable underlying central nervous system disorder, especially involving the brainstem or cerebellum, as well as the visual system, were excluded. None of the elected patients had a history of visual impairment. The control subjects were regular otorhinolaryngological patients who had no abnormalities of the visual, oculomotor and vestibular systems, nor of the central nervous system. Patients in the VA and control groups did not use any medication that might have interfered with the evaluation of vestibular and/or OKN responses.

2.2. Methods

2.2.1. Eye movement recording and calibration

For recording eye movements, d.c. electronystagmography (ENG) was applied, using a paper strip chart recorder. Eye movement was calibrated before and after each test by having the patient or subject look at a light dot which appeared in alternation at 10° on either side of the primary position.

2.2.2. OKN test

OKN responses were elicited with moving shadow stripes (7.5° width and separation), projected onto a hemicylindrical screen in front of the patient, which covered 90 × 50° (width x height) of the visual field. The patient was seated in a rotatory chair with the head supported by a headrest and with the interocular axis intersecting the long axis of the cylindrical screen, on which the projection drum was centered with the light bulb inside. The vertical axis of rotation of the stimulus was at about 125 cm distance from the cylindrical screen (Tönnies AG, Freiburg, Germany). Velocity-step stimulation was applied for at least 30 sec in each direction. The stimulus direction was repeatedly changed, especially if the patient's response showed a tendency to decline. There were no signs of gradual build-up of any of the responses. Only clear, steady responses were evaluated. Calibration and stimulation were performed without corrective glasses (as in spectacles), even if the patient normally wore such

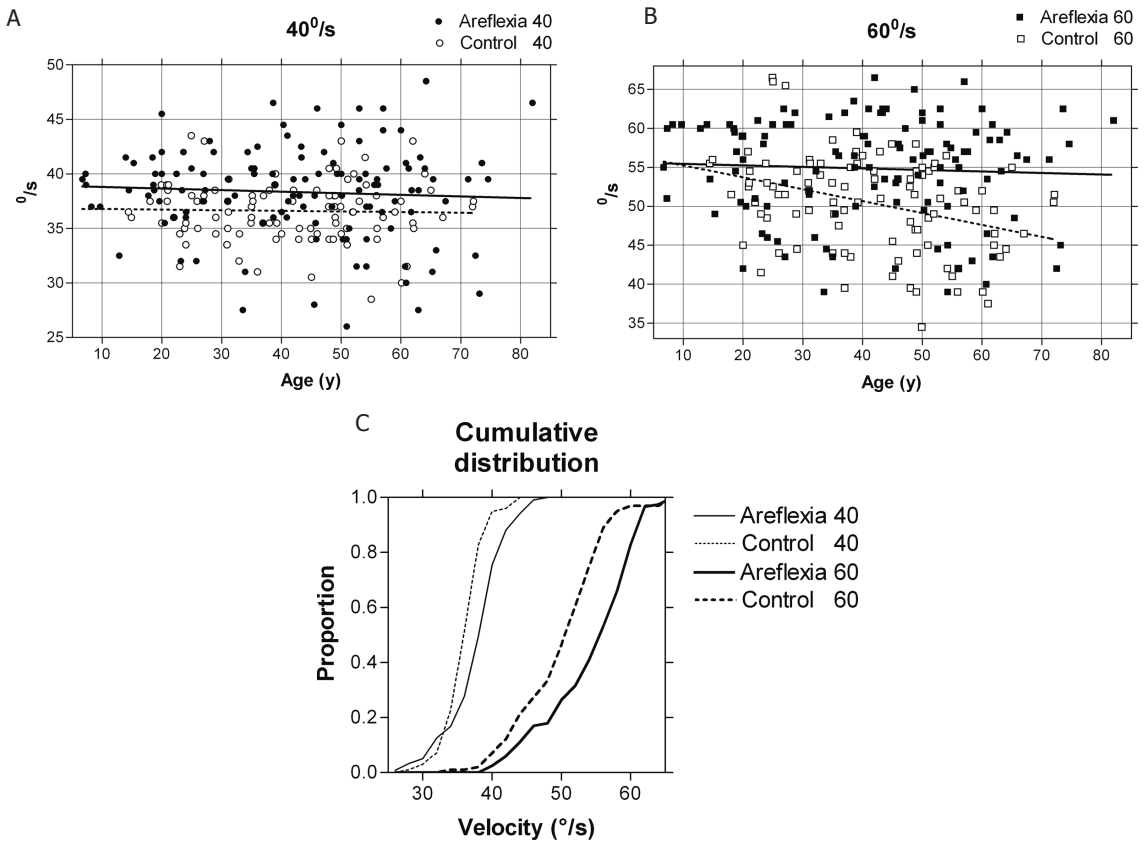

Fig. 1. OKN response velocity at 40°/s (A) and 60°/s (B) stimulation versus age (years) and the corresponding cumulative frequency distributions (C). The mean response velocity for the two nystagmus directions is plotted for the control subjects (open symbols) and for the VA patients (filled symbols). The continuous lines pertain to the VA patients and the dashed lines to the control subjects. Note wider scattering of the response levels and the clear bias towards higher values (gain $\geqslant 1$) in the group of VA patients. Slope was shallow and the correlation coefficient was significant only in the control group at 60°/s.

glasses [5]; it should be noted that blurring of OKN stimuli does not appreciably influence OKN gain [26]. The stimulus velocities used were 40 and 60°/s. The patients/subjects were instructed to look at the screen and not to try to follow specific stripes. For each stimulus direction, the mean SPV of 3 nystagmus beats was derived from (a part of) the constant-velocity response that showed optimal performance, most often at the point where the SPV had stabilized; this judgment was made "by eye". The OKN response velocity was taken as the bidirectional mean SPV.

2.2.3. Statistical analysis

Differences in the relative frequency of any feature were tested in a 2×2 contingency table, using a chi-squared test with Yates' correction. The Kolmogorov-Smirnov test was used to see whether any of the frequency distributions involved deviated significantly from a normal (Gaussian) distribution. Outlying values were detected by using Chauvenet's criterion [10]. Student's t test was used for comparing any relevant two categories, using the Welch-corrected variant in case the variances differed significantly (Bartlett's test, $P < 0.05$). Linear regression analysis was performed on the response-by-age data. Moreover, using the F test options of the Prism program, GraphPad, San Diego, it was tested whether the slopes between any relevant regression lines were significantly different ($P < 0.05$). If this was not the case, an F test was then performed in order to find out whether the intercepts were significantly different.

3. Results

The OKN response data for 40 and 60°/s stimulation and regression lines of SPV against age for both stimulus velocities are shown in Fig. 1. The mean

Table 2
Regression analysis for mean SPV on age. Test result relates to the F test mentioned in section 2.2.3. **Bold values indicate significant findings**

	VA 40°/s	Control 40°/s	VA 60°/s	Control 60°/s
n	119	98	117	99
Slope (°/s/y)				
Mean	−0.015	−0.0055	−0.020	**−0.153**
SD	0.022	0.020	0.035	0.042
Y-intercept (°/s)				
Mean	**38.95**	**36.81**	**55.63**	**56.77**
SD	1.02	0.87	1.57	1.84
r	−0.061	−0.028	−0.052	**−0.346**
Sy.x (°/s)	4.30	2.77	6.58	5.87
Test result	slopes ns	**intercepts S**	**slopes S**	intercepts na
Mean (°/s)	38.33	36.59	54.82	50.46
SD	4.28	2.76	6.56	6.23
SEM	0.39	0.28	0.61	0.63
Difference between means (°/s)		**1.74**		4.36
SD		0.48		0.87
95% CI		0.8 to 2.7		2.7 to 6.1

CI, confidence interval; na, not applicable (not calculated because slopes/lines are significantly different); ns, not significant; r, correlation coefficient; S, significant; SD, standard deviation; SEM, standard error of mean; Sy.x, residual SD for the regression of Y on X.

response velocity for the two nystagmus directions is plotted against age for the control subjects (open symbols) as well as for the VA patients (filled symbols). The relevant statistics are presented in Table 2. All four velocity distributions (Fig. 1C) passed the normality test and could be considered as Gaussian in first approximation, i.e. after removal of 1 outlying value from the control group at 40°/s (63 years/46.5°/s) and 3 outlying values from the VA group, all originating from poor responses. We were only able to reliably measure a few SPV values in these subjects: 19.5°/s for a 32-year-old patient at 40°/s stimulation, 20°/s for a 63-year-old patient, and 34°/s for a 65-year-old patient, both at 60°/s stimulation. One of these outliers related to the only VA patient who might be designated as a "poor responder"; in his case, VA was presumably caused by otosclerosis and he showed OKN response levels which at both stimulus velocities were $<$ the mean -2SD of the control group. His response at 40°/s (mean 27.5°/s) started with some nystagmus beats with an SPV of 36°/s, but declined thereafter.

The negative slopes (response level declining with advancing age) were all very shallow. None of the correlation coefficients was significant (i.e. slope significantly non-zero), except that for the control subjects at 60°/s. There was a significant difference in slope between the VA group and the control group at 60°/s stimulation (Fig. 1B, Table 2) which was related to increasing age (Fig. 1B). The mean response levels differed significantly between the VA group (higher values, see Fig. 1A,B) and the control group by approximately 1.7°/s at 40°/s and 4.4°/s at 60°/s stimulation (Table 2 and Fig. 1C). Although at both stimulus levels the Y intercepts appeared to differ significantly (separate t tests), the differences were small (Table 2). We were not able to detect any significant differences in response level between the categories of VA patients with normal hearing and those with complete deafness.

The data of the VA patients showed a wider scattering than those of the control subjects (Fig. 1A,B), which was also reflected in significant differences between the residual SDs (Sy.x in Table 2, test results not shown). There were significantly more cases with gain $\geqslant 1$ in the VA group than in the control group. In the control group, at 40°/s stimulation, only 11% of the responses (11 out of 99) showed such a high gain, while in the VA group 38% of the responses (46 out of 120) did. At 60°/s stimulation, 3% (3 out of 99) and 28% (33 out of 119) of the cases respectively, had such a high gain. There was no remarkable relationship between excessively high OKN gain and any specific aetiology. In the patient categories of bilateral normal hearing ($n = 15$) and bilateral deafness ($n = 42$), 27–29% had a gain of $\geqslant 1$.

The present observations clearly contradict the findings of prior studies (see Introduction) that the OKN response level is consistently lower in VA subjects.

4. Discussion

4.1. Age and response level in normal subjects

A significant negative correlation between the OKN response level and age was found at 60°/s in the control subjects, as others did before [1,25,29,37]. Paige measured the gain of sinusoidal smooth pursuit (SP, at 50°/s maximum velocity, 0.25 Hz) and OKN (full-field projection at 50°/s maximum velocity and 0.025–0.25 Hz with the instruction to attend the stripes) in 3 age classes [25]. The mean gain for these fast (cortical) responses was about 0.83, 0.75 and 0.64 in the young, middle-aged and elderly groups, respectively (age was not specified), for both stimulus modalities. He suggested similarities between the dynamics of the SP and OKN responses, which in our opinion might be caused by the instruction for the OKN test (instruction to follow the stripes).

4.2. Age and response level in our VA patients

At both stimulus velocities, our VA patients did not show a significant decrease in response level with increasing age. The difference in response level between the VA group and the control group was small but significant; the VA group showed higher response levels at both velocities. The difference was more pronounced at an older age and with higher stimulus velocity. We are curious about why VA patients do not show the decrease in OKN response level with advancing age that has been documented in healthy subjects. We can only speculate that, in order to maintain stability, they depend more heavily on the quality of their OKN response than healthy subjects and that they cannot really "afford" such a decrease in response (whatever its cause in controls) which, regarding their (special) condition, may jeopardize their stability.

An association between VA and diminished OKN responses, which was previously suggested by others (see Introduction), was not confirmed by our study. Yet, one should realize that we excluded some poor responders. This was however only done if we had the impression that the patient, who was not suspected to have any central abnormality, did not perform optimally in the OKN test. It is perfectly clear that patients having VA next to specific central lesions may respond poorly to OKN stimulation, as will be discussed in section 4.4.

4.3. OKN gain > 1?

The finding of OKN responses with an apparent gain $\geqslant 1$ is puzzling. It occurred both in subjects with and without VA, but significantly more often in the latter category. A trivial but plausible explanation of such findings can be based on the inherent, substantial variability in gain, which is even greater in the VA group, combined with a shift in mean gain towards higher values in this group. We cannot exclude the possibility that greater instability in the SPV of the OKN responses of VA patients, as compared with the controls, accounts for the greater variability as demonstrated by the wider scattering in Fig. 1. The higher response level in the VA group is discussed below.

Sources of instrumental errors include the measurements, calibration amplitude and slope tangent readings as well as a relatively rapid change in corneoretinal potential in between the (preceding and following) calibrations. One might suppose that the exact gain was $\leqslant 1$ but that the accumulation of the above-mentioned type of errors resulted in the appearance of values with gain > 1.

Systematic instrumental errors may have been associated with the geometry of stimulation. We have previously stipulated the fact that the vertical axis of rotation of the stimulus was at about 125 cm distance from the cylindrical screen and that the eyes are about 12 cm closer to the screen than the vertical axis of rotation of the skull [18]. This implies that the real stimulus velocities may have been higher than the intended stimulus velocities of 40 and 60°/s.

From Cannon et al.'s report, it can be derived that a hyperope's VOR which adapts to the use of plus 4 diopter (4D) lenses during head movement will show an increase in the gain of compensatory eye movements of about 10% [5]. However, as was recommended by these authors, we did not allow the patients or controls to use their glasses during calibration and OKN stimulation.

4.4. OKN response level in human studies on VA

This study shows that the OKN gain can be maintained or even increased in the absence of labyrinthine function; other studies have reported a decrease [3,38, 39]. We do not suppose that our stimulus conditions differed substantially from those employed by Zee et al. or Bles et al. [3,39], while Zasorin et al. [38], who used a velocity of 30°/s with the instruction to "stare", obtained results similar to Zee et al. [39]. We previ-

ously suggested [17] that in VA patients the observed enhancement of the cervico-ocular reflex (COR) depends on the presence of an intact OKN/SP system and that this would explain why Leopold et al. [23] failed to find any substantial COR enhancement in their patients, most of whom combined VA with defective OKN/SP responses due to central nervous system disorders. Similar findings of a lack of COR enhancement have been reported by Bronstein et al. in patients (with multisystem atrophy) who had similar combined dysfunctions [4]. Waterston et al. studied compensatory eye movements (CEM) during head-free and head-fixed pursuit in similar patients and in patients with only VA. They found no difference in CEM between head-free and head-fixed conditions in patients with only VA, but in the patients with additional failure of OKN/SP due to involvement of cerebellar pathways, CEM could not be elicited [36]. Bronstein et al. stated that the patients with combined failure might have had such widespread neural damage that it was impossible to reliably indicate the site of the lesion responsible for the lack of gain enhancement [4].

4.5. Speculations about OKN response level in human studies on VA

In the past, interesting speculations have been made about decreased OKN responses in VA. On account of the present findings we will now speculate on increased OKN responses.

4.5.1. Speculations about decreased OKN response level in human studies on VA

It has been suggested that reduced OKN responses are consequential to a lack of activity of primary afferent vestibular neurons after the loss of peripheral vestibular function. This speculation, as was previously elaborated on by others [38,39], is based on the notion that the secondary (central) vestibular neurons form part of the "velocity storage mechanism", which was originally conceived by Cohen et al. [6] and Raphan et al. [28] to explain their findings in the monkey. The velocity storage mechanism is supposed to be shared by the VOR and the subcortical optokinetic system see for review [2,8,19,27].

4.5.2. Speculations about increased OKN response level in human studies on VA

Human subjects without vestibular function undergo more intense optokinetic stimulation during their daily life activities than healthy subjects. Leigh et al. found evidence that, in a condition of whole body rotation with simultaneous visual fixation of a stationary target, the SP system is only recruited in VA patients, but not – or to a much lesser extent – in healthy subjects, whose VOR is activated [22]. Although compensatory processes utilizing compensatory eye movements produced by "central (pre)programming" [9,11,21] or the cervico-ocular reflex (COR) [17] maybe involved, the reduction of retinal slip during head movement in the absence of labyrinthine function will generally be less effective than with the normal VOR [21,30]. It can be speculated that an increase in retinal slip, which in VA patients is due to the absence of the VOR, favours the development of more efficient signal processing by an alternative pathway, if such a pathway is available, and if it has the capacity to improve its performance. In primates, the cortical optokinetic system seems to be a good candidate for developing such a pathway. The finding by Miyoshi and Pfaltz [24] that OKN training (in normal subjects) leads to an increase in OKN gain, see for review [8] suggests cortical involvement, although there may be cerebellar influences as well. In the natural condition of active head movements, it seems possible that (other?) central systems can also make use of an "efference copy" to improve overall performance.

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References

[1] R.W. Baloh, K.M. Jacobson and T.M. Socotch, The effect of aging on visual-vestibuloocular response, *Experimental Brain Research* **95** (1993), 509–516.

[2] G.R. Barnes, Visual-vestibular interaction in the control of head and eye movement: the role of visual feedback and predictive mechanisms, *Progress in Neurobiology* **41** (1993), 435–472.

[3] W. Bles, J.M.B.V. de Jong and J.J. Rasmussens, Postural and oculomotor signs in labyrinthine-defective subjects, *Acta Otolaryngolica* (*Stockholm*) **406** (1984), 101–104.

[4] A.M. Bronstein, S. Mossman and L.M. Luxon, The neck-eye reflex in patients with reduced vestibular and optokinetic function, *Brain* **114** (1991), 1–11.

[5] S.C. Cannon, R.J. Leigh, D.S. Zee and L.A. Abel, The effect of the rotational magnification of corrective spectacles on the quantitative evaluation of the VOR, *Acta Otolaryngologica* (*Stockholm*) **100** (1985), 81–88.

[6] B. Cohen, V. Matsuo and T. Raphan, Quantitative analysis of the velocity characteristics of optokinetic nystagmus and optokinetic after-nystagmus, *Journal of Physiology* (*London*) **270** (1977), 321–344.
[7] B. Cohen, T. Uemura and S. Takemori, Effects of labyrinthectomy on optokinetic nystagmus (OKN) and optokinetic after-nystagmus (OKAN), *Equilibrium Research* **3** (1973), 88–93.
[8] H. Collewijn, Integration of adaptive changes of the optokinetic reflex, pursuit and the vestibulo-ocular reflex, in: *Adaptive Mechanisms in Gaze Control. Facts and Theories*, A. Berthoz and G. Melvill Jones, eds, Elsevier, Amsterdam/ New York/ Oxford, 1985, pp. 51–69.
[9] J. Dichgans, E. Bizzi, P. Morasso and V. Tagliasco, Mechanisms underlying recovery of eye-head coordination following bilateral labyrinthectomy in monkeys, *Experimental Brain Research* **18** (1973), 548–562.
[10] Documenta Geigy, *Scientific Tables*, (5th ed.), S Karger, Basel/New York, 1959, p. 47.
[11] M.A. Gresty, K. Hess and J. Leech, Disorders of the vestibular reflex producing oscillopsia and mechanisms compensating for loss of labyrinthine function, *Brain* **100** (1977), 693–716.
[12] T.C. Hain and D.S. Zee, Abolition of optokinetic afternystagmus by aminoglycoside toxicity, *Annals of Otology, Rhinology and Laryngology* **100** (1991), 580–583.
[13] P.L.M. Huygen and R.J.C. Admiraal, Audiovestibular sequelae of congenital cytomegalovirus infection in 3 children presumably presenting 3 symptomatically different types of delayed endolymphatic hydrops, *International Journal of Pediatric Otorhinolaryngology* **35** (1996), 143–154.
[14] P.L.M. Huygen, J.B. Hinderink, P. van den Broek, S. van den Borne, J.P.L. Brokx, L.H.M. Mens and R.J.C. Admiraal, The risk of vestibular function loss after intracochlear implantation, *Acta Otolaryngologica* (*Stockholm*) **520** (1995), 270–272.
[15] P.L.M. Huygen, P.M. van Rijn, C.W.R.J. Cremers and E.J.J.M. Theunissen, The vestibulo-ocular reflex in pupils at a Dutch school for the hearing impaired; findings relating to acquired causes, *International Journal of Pediatric Otorhinolaryngology* **Suppl. 520** (1993), 39–47.
[16] P.L.M. Huygen and W.I.M. Verhagen, Peripheral vestibular and vestibulo-cochlear dysfunction in hereditary disorders: A review of the literature and a report on some additional findings, *Journal of Vestibular Research* **4** (1994), 81–104.
[17] P.L.M. Huygen, W.I.M. Verhagen and M.G.M. Nicolasen, Cervico-ocular reflex enhancement in labyrinthine-defective and normal subjects, *Experimental Brain Research* **87** (1991), 457–464.
[18] P.L.M. Huygen, W.I.M. Verhagen, E.J.J.M. Theunissen and M.G.M Nicolasen, Compensation of total loss of vestibulo-ocular reflex by enhanced optokinetic response, *Acta Otolaryngologica* (*Stockholm*) **Suppl. 468** (1989), 359–364.
[19] U.J. Ilg, Slow eye movements, *Progress in Neurobiology* **53** (1997), 293–329.
[20] D.J. Ireland and R.M. Jell, Optokinetic after-nystagmus in man after loss or reduction of labyrinthine function: A preliminary report, *Journal of Otolaryngology* **11** (1982), 86–90.
[21] T. Kasai and D.S. Zee, Eye-head coordination in labyrinthine-defective human beings, *Brain Research* **144** (1978), 123–142.
[22] R.J. Leigh, W.P. Huebner and J.L. Gordon, Supplementation of the human vestibulo-ocular reflex by visual fixation and smooth pursuit, *Journal of Vestibular Research* **4** (1994), 347–353.
[23] H.C. Leopold, M. Doerr and U. Thoden, Cervico-ocular responses (COR) during slow sinusoidal head movements in subjects with bilateral labyrinthine lesions, *Archiv für Psychiatrie und Nervenkrankheiten* **233** (1983), 439–447.
[24] T. Miyoshi and C.R. Pfaltz, Studies on optokinetic habituation, *Journal for Oto-Rhino-Laryngology and its Related Specialties* **34** (1972), 308–319.
[25] G.D. Paige, Senescence of human visual-vestibular interactions: smooth pursuit, optokinetic, and vestibular control of eye movements with aging, *Experimental Brain Research* **98** (1994), 355–372.
[26] R.B. Post, C.S. Redemer, J. Dichgans and H.W. Leibowitz, Dynamic orientation responses are independent of refractive errors. (ARVO abstract), *Investigative Ophthalmology and Visual Science* **Suppl. 18** (1979), 140–141.
[27] T. Raphan and B. Cohen, Velocity storage and the ocular response to multidimensional vestibular stimuli, in: *Adaptive Mechanisms in Gaze Control. Facts and Theories*, A. Berthoz and G. Melvill Jones, eds, Elsevier, Amsterdam/ New York/ Oxford, 1985, pp. 123–143.
[28] T. Raphan, V. Matsuo and B. Cohen, Velocity storage in the vestibulo-ocular reflex arc (VOR), *Experimental Brain Research* **35** (1979), 229–248.
[29] B. Simons and U. Büttner, The influence of age on optokinetic nystagmus, *European Archives of Psychiatry and Clinical Neuroscience* **234** (1985), 369–373.
[30] M. Takahashi, T. Uemura and T. Fujishiro, Compensatory eye movements and gaze fixation during active head rotation in patients with labyrinthine disorders, *Annals of Otolology, Rhinology and Laryngology* **90** (1981), 241–245.
[31] W.I.M. Verhagen, P.L.M. Huygen and W. Bles, A new autosomal dominant syndrome of idiopathic progressive vestibulocochlear dysfunction with middle-age onset, *Acta Otolaryngologica* (*Stockholm*) **112** (1992), 899–906.
[32] W.I.M. Verhagen, P.L.M. Huygen and M.W.I.M. Horstink, Familial congenital vestibular areflexia, *Journal of Neurology, Neurosurgery and Psychiatry* **50** (1987), 933–935.
[33] W.I.M. Verhagen, P.L.M. Huygen and E.M.G. Joosten, Familial progressive vestibulocochlear dysfunction, *Archives of Neurology* **45** (1988), 766–768.
[34] W.I.M Verhagen, P.L.M. Huygen, E.J.J.M. Theunissen and E.M.G. Joosten, Hereditary vestibulo-cochlear dysfunction and vascular disorders, *Journal of the Neurological Sciences* **92** (1989), 55–63.
[35] W. Waespe and M. Wolfensberger, Optokinetic nystagmus (OKN) and optokinetic after-responses after bilateral vestibular neurectomy in the monkey, *Experimental Brain Research* **60** (1985), 263–269.
[36] J.A. Waterston, G.A. Barnes, M.A. Grealy and L.M. Luxon, Coordination of eye and head movements during smooth pursuit in patients with vestibular failure, *Journal of Neurology, Neurosurgery and Psychiatry* **55** (1992), 1125–1131.
[37] D.H. Zackon and J.A. Sharpe, Smooth pursuit in senescence, Effects of target acceleration and velocity, *Acta Otolaryngologica* (*Stockholm*) **104** (1987), 290–297.
[38] N.L. Zasorin, R.W. Baloh, R.D. Yee and V. Honrubia, Influence of vestibulo-ocular reflex gain on human optokinetic response, *Experimental Brain Research* **51** (1983), 271–274.
[39] D.S. Zee, R.D. Yee and D.A. Robinson, Optokinetic repsonses in labyrinthine-defective human beings, *Brain Research* **113** (1976), 423–428.