

# Correlation between vestibulo-ocular reflex and optokinetic afternystagmus in normal subjects and in patients with vestibular system disorders

## Correlazioni tra il riflesso vestibolo-oculare e il nistagmo post-ottocinetico nei soggetti normali e in pazienti con patologia del sistema vestibolare

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### Key words

Vestibular disorders • Diagnosis • Vestibulo-ocular reflex  
 • Optokinetic afternystagmus

### Parole chiave

Disordini vestibolari • Diagnosi • Riflesso vestibolo-oculare • Post-nistagmo ottocinetico

### Summary

Optokinetic afternystagmus follows optokinetic nystagmus as an expression of the central velocity storage integrator discharge and its fast phase is beating in the same direction as the previous optokinetic nystagmus. We investigated the correlation between vestibulo-ocular reflex and optokinetic afternystagmus in normal subjects and in patients with bilateral vestibular disorders. The aim of this study was to determine the possible role of optokinetic afternystagmus as a diagnostic test for identifying functional vestibular disorders. The subjects were examined by electronystagmography and vestibulo-ocular reflex, optokinetic nystagmus stare type as well as optokinetic afternystagmus were recorded. They were restrained in a rotatory drum chair, both the chair and the drum could be rotated, independently or coupled. For vestibulo-ocular reflex analysis, we studied post-rotatory-nystagmus from a velocity of 90°/s. Optokinetic nystagmus was recorded at a drum velocity of 30°/s and the registration continued in total darkness, after the illumination was switched off, to study optokinetic afternystagmus. We considered vestibulo-ocular reflex and optokinetic nystagmus gain, vestibulo-ocular reflex and optokinetic afternystagmus constant of time (tc) defined as the time necessary for the slow phase eye velocity to be reduced to 37% of its initial value. Results demonstrated that vestibulo-ocular reflex gain and tc showed a significant difference only in patients with reduced vestibular reflexia, while optokinetic nystagmus gain was greater only in patients with increased reflexia; optokinetic afternystagmus tc was different from the control group only in patients with hyporeflexia. In conclusion, our results suggest that vestibulo-ocular reflex and optokinetic afternystagmus tc are clinically more useful than the gain alone in testing vestibular disorders with hyporeflexia. On the other hand, we propose a new mathematical and statistical approach to study the temporal evolution of more parameters of the nystagmus.

### Riassunto

Il post-nistagmo ottocinetico (OKANI) compare dopo il nistagmo ottocinetico (OKN), è dovuto alla scarica di strutture nervose responsabili dell'accumulo di velocità (velocity storage) e la sua fase rapida batte nella stessa direzione del precedente OKN. Abbiamo studiato la correlazione tra il riflesso vestibolo-oculare (VOR) e il post-nistagmo ottocinetico in soggetti normali e in pazienti con alterata riflessia vestibolare bilaterale allo scopo di verificare l'utilità diagnostica dell'OKAN nella valutazione della funzionalità vestibolare. I soggetti sono stati esaminati con metodo elettronistagmografico, seduti su una sedia rotatoria entro un cilindro che può ruotare indipendentemente o sinergicamente alla sedia stessa, per lo studio del VOR, dell'OKN di tipo stare e dell'OKANI. Lo studio del VOR è stato effettuato sul nistagmo post-rotatorio dopo Stop-test da una velocità di 90°/sec.; l'OKN è stato studiato con una velocità di rotazione del cilindro di 30°/sec. per 60 sec. e l'osservazione è stata protratta al buio, dopo lo spegnimento della luce, per la valutazione dell'OKANI. Abbiamo preso in considerazione il gain del VOR, il gain dell'OKN e la costante di tempo (tc), definita come il tempo necessario perché la velocità angolare della fase lenta diminuisca sino al 37% del suo valore originale. Dai risultati emerge che il gain e la tc del VOR risultano variare significativamente solo nei soggetti con diminuita riflessività vestibolare, mentre il gain dell'OKN è significativamente maggiore solo in presenza di aumentata riflessività, come pure la tc del VOR; invece la tc dell'OKANI varia significativamente solo nei pazienti con iporefflessia vestibolare. In conclusione, sebbene la tc del VOR e dell'OKANI abbiano un analogo comportamento per lo meno nei soggetti con diminuita riflessività vestibolare e possono essere considerati un indice clinico più affidabile rispetto al gain, riteniamo più utile ai fini diagnostici un nuovo metodo per lo studio del nistagmo basato su un'analisi matematica e statistica di più parametri analizzati nella loro evoluzione temporale.

## Introduction

Primary optokinetic afternystagmus (OKAN) follows the optokinetic nystagmus (OKN), which is triggered by image slip on the retina when visual stimulus is terminated by complete darkness.

During the optokinetic stimulation, activity related to slow phase eye velocity (SPEV) in the subcortical pathways is stored by the central velocity storage integrator<sup>1-3</sup>, which discharges, generating OKAN1 with fast phases beating in the same direction as the previous OKN<sup>4</sup>.

OKAN1 is sometimes followed by a secondary optokinetic afternystagmus (OKAN2) moving in the opposite direction<sup>4</sup>. The meaning of this reversal phase is still obscure although it has been suggested to be caused by central nervous system (CNS) adaptation to the optokinetic stimulus<sup>5,6</sup>.

The relevance of the vestibular system, on the genesis of the OKAN, is supported by several studies. Peripheral vestibular lesions may cause a loss of symmetry in the primary and secondary OKAN with a decrease in the strengths expressed by the gain and duration<sup>7-9</sup>.

Moreover, optokinetic after-response, in such cases, is asymmetric with the OKAN1 beating toward the pathologic ear being significantly weaker than the OKAN1 beating toward the healthy ear<sup>7-10</sup>.

It has been suggested that the appearance of directional asymmetry and/or a reduced time constant of optokinetic afternystagmus (OKAN tc) might be a clinical index of vestibular imbalance<sup>11,12</sup>. To test this hypothesis, we studied changes both in the gain of the vestibulo-ocular reflex (VOR) and OKN and in the time constants of the VOR and OKAN in patients with vestibular system disorders. The study design allowed information to be obtained concerning the clinical relevance of the OKAN tc.

## Materials and Methods

### SUBJECTS

A total of 38 subjects (21 male, 17 female, age range 22-76 years, mean 51), with vestibular disorders who showed a bilateral vestibulopathy were submitted to electronystagmographic examination. Of these, 23 presented combined vestibular loss and uni- or bilateral auditory loss. None showed spontaneous nystagmus or had taken sedating medications within 48 hours before testing.

Clinical history included chronic persistent or recurrent dizziness in 24 cases, associated with vertigo and neurological signs in 4 other subjects and only neurological symptoms in another 2 patients. The remaining 8 subjects did not complain of vestibular symptoms from 6 to 20 months, at the time of the ex-

amination. A specific diagnosis was made in 25 cases and included chronic otitis in 3 patients, of traumatic aetiology in 4 cases, previous exposure to known ototoxic drugs in 10, vertebral insufficiency and/ or cerebellar pathology in 8.

As a control group for ENG data, 20 healthy adults were identified.

Three groups of subjects were enrolled in the study. Group 1: 20 healthy adults (12 male, 8 female, aged 24 to 27 years, mean 25.2). None had a history of past or present neurological, ophthalmologic, otologic, systemic, or traumatic disease that could potentially have affected results.

Group 2: 18 patients (11 male, 7 female; aged 22 to 70 years, mean 53) with bilateral vestibular hyperreflexia.

Group 3: 20 patients (10 male, 10 female; aged 30 to 76 years, mean 48) with bilateral peripheral hyporeflexia.

### APPARATUS

Subjects were restrained in an electrically operated drum chair (Tönnies GmbH & Co., Würzburg, Germany). The chair rotated about the axis of a surrounding cylindrical drum, 20 m diameter and 1.90 m in height. On the inner wall of the drum were 32 vertical black stripes, 9.32 cm in width and at an angle of 5°, 61 each were painted on a white background. The moving pattern filled the entire visual field. Both the chair and the drum could be rotated (independently or coupled) at computer-controlled velocities. With the illumination switched off, the drum ensured total darkness for isolated testing of the VOR with eyes open.

Horizontal eye movements were recorded by surface electrodes located on the outer edge and printed using a polygraph (Tönnies GmbH & Co., Würzburg, Germany) with a paper speed of 5 mm/s.

Data were introduced and then analyzed by Lab-View 4.0 software (National Instruments, Austin, TX, USA).

### PROCEDURE

For VOR analysis, subjects were rotated at a velocity of 90°/s reached by subliminal acceleration in 190 s and then maintained for 30 s. This was done both clockwise and counterclockwise.

After 30 s of rotation at 90°/s the seat was stopped and nystagmus were recorded in total darkness.

We studied the OKN stare type. The drum was rotated at a velocity of 30°/s for 60 s both clockwise and counterclockwise. After each stimulation, the illumination was switched off for nystagmus recording. Subjects were asked to look at stripes on the internal wall of the drum but without fixing.

A pause of 300 s was taken between stimulations. Calibration of eye movements was performed en-

couraging subjects to follow a light moved across the visual field ( $1 \text{ mm} = 10^\circ$ ).

### ANALYSIS

For the analysis of recordings, gain and tc were obtained both manually and by means of computerized analysis.

VOR gain was defined as the ratio of the maximal SPEV of the eyes to the maximal head rotation velocity and it was calculated from the first three nystagmic eye movements.

Tc was defined as the time necessary to achieve a 37% reduction of the initial value.

OKN gain was calculated for the first 20 s (mean of a group of nystagmic movements of at least 3 in 5 s) since, in this time period, OKN develops better and without fatigability phenomenon. For the analysis of OKAN, we calculated tc without taking into consideration the first 2 s after optokinetic stimulus was abolished, by darkness, to exclude the break point between OKN and OKAN<sup>12</sup>.

The OKAN gain was not calculated since it could simply represent the continuation of OKN with a decreasing SPEV and, therefore, its gain value may be considered as the OKN gain value.

Statistical analysis was performed using Bonferroni's T test.

### Results

We analyzed VOR, OKN, OKAN1 and differences between VOR gain and OKN gain; VOR tc and OKAN1 tc in the 3 groups (Figs. 1, 2 and Tables I, II).

VOR gain and tc in subjects with bilateral vestibular hyperreflexivity were greater than in the control group, but only VOR tc showed a significant difference ( $p < 0.05$ ), while both were reduced ( $p < 0.05$ ) in the group with bilateral vestibular hyporeflexia.

OKN gain in patients with bilateral vestibular hyperreflexivity was greater than in normal subjects ( $p < 0.05$ ), but in patients with bilateral vestibular hyporeflexia, there was no significant difference vs. the control group.

OKAN1 tc was no different from that in group 1 in patients with bilateral vestibular hyperreflexia ( $p > 0.05$ ). In patients with bilateral vestibular hyporeflexia, a significant difference was observed vs. the control group and group 2 ( $p < 0.05$ ).

### Discussion

Table III reports no published data acquired on the OKAN1 presence of total 998 subjects with normal or pathological vestibular reflexia. It is interesting to

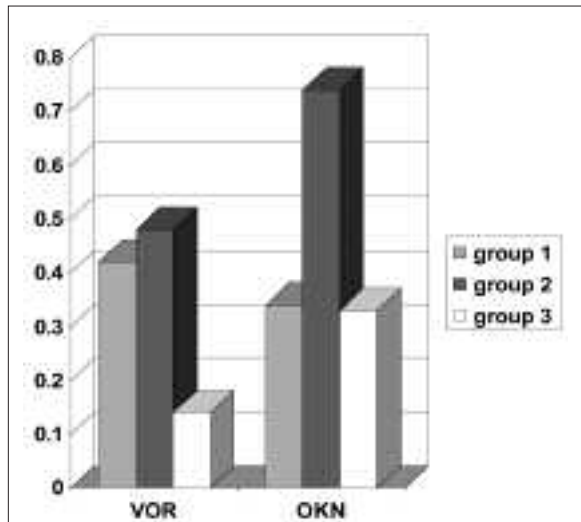


Fig. 1. Gain

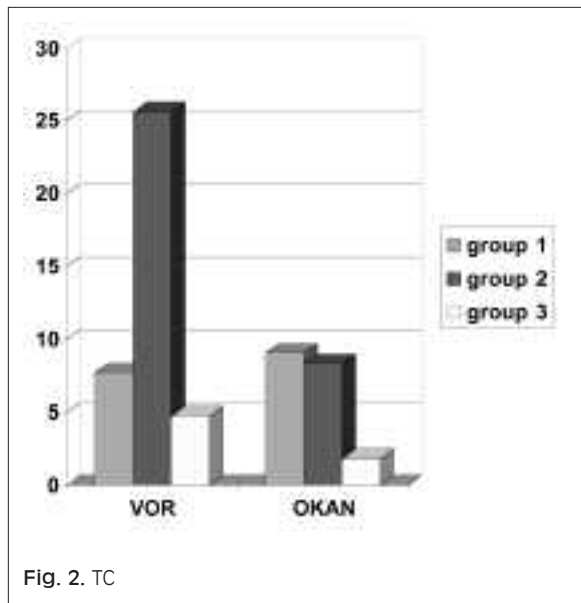


Fig. 2. TC

note the OKAN evidence in 736 subjects, 94.6% showing vestibular hyperreflexia, 54.48% hyporeflexia and 72.88% normal vestibular reflectivity.

The most important result emerging from this study was the finding that the gain and TC VOR and the TC OKAN1 were significantly reduced in the patients with bilateral vestibular loss. This result emphasizes that the vestibular system plays an important role in the genesis of OKAN<sup>12-14</sup>.

In the same group, no variation in OKN gain was observed, according to Barkley et al. (1989), while in

**Table I.** Mean value and standard deviation of VOR and OKN gain and VOR and OKAN time constant (TC) in patients with vestibular hyperreflexia (group 2), vestibular hyporeflexia (group 3) and in normal subjects (group 1).

Gain				
Group	VOR mean	SD	OKN mean	SD
1	0.42	0.12	0.34	0.007
2	0.48	0.12	0.74	0.15
3	0.14	0.14	0.33	0.090
TC				
Group	VOR	SD	OKAN	SD
1	7.70	3.34	9.03	6.21
2	25.60	9.19	8.29	5.13
3	4.71	2.83	1.79	1.95

**Table II.** Bonferroni's T test results. The difference between constant of time (ct) of the OKAN in patients with vestibular hyperreflexia and control group is not significant.

Group	T test results for VOR and OKN gain		T test results for VOR and OKAN ct	
	VOR	OKN	VOR	OKAN
2 vs. 1	p > 0.05	p < 0.05	p < 0.05	p > 0.05
3 vs. 1	p < 0.05	p > 0.05	p < 0.05	p < 0.05
2 vs. 3	p > 0.05	p < 0.05	p < 0.05	p < 0.05

**Table III.** Presence/absence of OKAN in 998 subjects with normal or pathological vestibular reflexia.

	OKAN present	OKAN absent
Vestibular hyperreflexia	330 (94.6%)	22 (6.4%)
Vestibular hyporeflexia	242 (57.48%)	179 (42.51%)
Vestibular normoreflexia	164 (72.88%)	61 (27.11%)
Total	736 subjects	262 subjects

patients with bilateral vestibular hyperreflexia and VOR gain with no significant difference vs. group 1, OKN gain was higher than in normal subjects. Moreover, differences between VOR constant of time in normal subjects and both in patients with bilateral hyperreflexia and hyporeflexia were significant ( $p \leq 0.05$ ). These results suggest that VOR gain alone may not be clinically useful in testing vestibular disorders, while VOR constant of time, which studies the temporal evolution of nystagmus, appears to be a more valid clinical parameter.

On the other hand, when considering the OKAN1 tc, we observed that this is not a suitable parameter to

distinguish between normal subjects and patients with vestibular hyperreflexia ( $p > 0.05$ ).

We conclude that OKAN1 tc might be useful for clinical purposes, combined with the other subtests, such as VOR tc, only in bilateral vestibular loss.

On account of these observations, we propose a new mathematical and statistical approach to study the temporal evolution of nystagmus. With temporal analysis, it is possible to estimate both the SPEV, both the fast phase eye velocity (FPEV) and their inter-relationship. Preliminary results have been reported elsewhere<sup>15</sup>.

A more detailed analysis of nystagmus induced by

vestibular and/or retinic stimulation, based on the study of more parameters and their temporal evolu-

tion, is consistent with the anatomical and functional complexity of the OKN, VOR interaction.

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