

# Asymmetry of visuo-vestibular mechanisms contributes to reversal of optokinetic after-nystagmus

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**Abstract** When the visual background is moving while subject fixate a visual target, optokinetic eye movements (OKN) are suppressed and the after response, called optokinetic after nystagmus (OKAN), occurring at the stimuli offset is often inverted as compared to the situation when the OKN movements are allowed. In this study, we investigated whether this reversal of OKAN results from a perceptual or extra-retinal feedback in relation with the pursuit system and/or the vestibular indirect system. Optokinesis performance was studied in normal subjects in four experiments always using the same background motion (1) to characterize the OKN and OKAN performance elicited by the whole visual field motion while fixating or not a central visual target, (2) to investigate the 3D characteristics of the OKAN reversal by using different orientations of the visual stimulation, (3) to correlate the occurrence of an inverted OKAN with functional asymmetry of the visuo-vestibular system, by studying the effects of ocular fixation deviations and finally (4) to examine the effects of the depth plane of gaze fixation on the OKAN characteristics. In Experiments 1 and 2, we observed that the visual fixation during full-field motion induced either a dumping effect or an inversion

of the OKAN response that could occur in the different planes of eye movements. The time constant was significantly increased in the inverted after-responses as compared to the not inverted ones. In Experiment 3, we found that the occurrence of an OKAN reversal after eye movement inhibition was significantly related to the presence of right/left asymmetrical OKAN responses. Moreover, the OKAN time constant was strikingly dependent on the eye fixation position during the visual stimulation and this time constant/eye position relation diverged between OKAN responses with and without inversion. Finally, Experiment 4 showed that the OKAN inversion tended to disappear when the visual target to fixate was in the near space as compared to the far space included in the background. These results argue in favor of an extraretinal influence in relation to the dynamics of the vestibulo-motor system, rather than for a perceptual influence on the inverted OKAN mechanisms. More precisely, we postulate that the reversal of OKAN could be linked to an inhibition issued from pursuit signals combined with an asymmetrical activity in the VSM vestibular complex.

**Keywords** OKAN inversion · Visual motion · Gaze fixation · Pursuit · Velocity storage · Human

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## Introduction

During head and body displacements, the maintenance of visual stability is realized by different stabilization systems including the vestibular system, compensating for head motion in interaction with the visual system compensating for retinal slip. The visual system can be triggered either by object displacements inducing an ocular visual pursuit or by large visual field displacements inducing alternated slow

and fast eye movements called optokinetic nystagmus (OKN). While the ocular pursuit provides a foveation of a moving object, the OKN slow component combined with the vestibulo-ocular reflex, compensates for the retinal slip thus providing stabilization of the visual world on the retina.

In the experimental condition, after the extinction of the visual stimulus, OKN can be prolonged in the dark, thus forming an after response (OKAN: optokinetic after-nystagmus) with slow movements in the same direction as the visual stimulus. Sometimes, OKAN (I) can be followed by a second OKAN (II) beating in the opposite direction. Evidence has been provided for two sub-systems underlying OKN and OKAN generation: (1) One is responsible for the rapid rise and release, respectively, of the OKN and OKAN velocities and is mediated by direct pathways linked to the smooth pursuit system and (2) another is responsible for the secondary slow rise and steady-state of OKN velocity as well as for the OKAN velocity decline mediated by indirect vestibular pathways (Ilg 1997, for review). During an optokinetic stimulation (large visual field motion), the indirect component would charge eye velocity signals thus contributing to the OKN velocity build-up. At the stimulus extinction, the discharge of the eye velocity storage would maintain the eye response, accounting for the OKAN. Such a discharge of the velocity storage—called the velocity storage mechanism—(VSM) yields the time constant of the OKAN response. The VSM constitutes a multimodal structure involving the vestibular nuclei complex. It is triggered either by visual (optokinetic) or vestibular inputs and is implicated in the sensation of circularvection (Cohen et al. 1977; Lafortune et al. 1986; Waespe and Schwartz 1986; Cannon and Robinson 1987).

In condition of gaze fixation or pursuit of a visual target against the moving background, there has been described a cancelation of OKN responses either by perceptual feedback from the relative target/background motion (Wyatt and Pola 1984; Suehiro et al. 1999; Kodaka et al. 2004) or by extra-retinal inputs from the smooth pursuit system (Pola et al. 1995; Lindner and Ilg 2006). Interestingly, after such OKN inhibition, OKAN is still present and often occurs with a reversal of the slow components in the opposite direction of the visual stimulus (Brandt et al. 1974; Kudo et al. 2002). The origin of such a reversal of the after response has been sparsely investigated. Brandt et al. (1974) described the OKAN inversion as a central counter-regulation due to motion habituation. Indeed, these authors correlated the presence of inverted after-response with long duration of optokinetic stimulation (>3 min). More recently, Kudo et al. (2002) suggested that the reverse OKAN is generated by a perceptual mechanism fed by the retinal slip during the optokinetic stimulation and that would involve the VSM generating the OKAN. To date, questions remain open concerning the exact mechanisms

responsible for such an inverted after-response occurring after gaze fixation during background motion.

In this study, we investigated the OKAN characteristics in different experimental conditions in an attempt to better understand the underlying mechanisms involving (or not) the pursuit system and/or the VSM indirect system. For this purpose we studied the optokinesis performance in normal subjects over four experiments always using the same background motion (1) to characterize the OKN and OKAN performance elicited by the whole visual field motion while fixating or not a central visual target, (2) to investigate the 3D characteristics of the OKAN reversal by using different orientations of the visual stimulation (3) to correlate the occurrence of an inverted OKAN with functional asymmetry of the visuo-vestibular system, including the VSM and finally (4) to study the effects of the depth plane of gaze fixation on the OKAN, including a reversal occurrence.

## Materials and methods

### Subjects

A total of 23 right-handed healthy subjects (mean age = 26; SD 6; 13 males, 10 females) participated in Experiment 1, 14 out of the 23 subjects (mean age: 28, SD 7; 6 males, 8 females) in Experiment 2 and 9 out of the 23 subjects (mean age = 23.8, SD 2.5; 6 males, 3 females) in Experiments 3 and 4. All were free of any vestibular and ocular pathologies and of neurological diseases. Prior to any vestibular testing, they were fully informed about the examination and gave their consent to participate in the study. The experimental protocols were duly approved by the local ethic committee at Lyon Hospital (CCPRB Lyon A).

### Experimental setup

The subject was comfortably seated in the dark in front of a semi-circular white screen (1 m radius) on which was projected a moving pattern of random dots issued from an illuminated perforated sphere that could rotate around different axes. The center of the head was positioned and maintained by a concave head rest and a frontal support at the center of the stimulus rotation axis. The 3D position of the left eye was recorded by video-oculography (VOG, SensoMotoric Instruments, Teltow, Germany). The VOG system used a remote head miniaturized CCD video sensor fixed on a head-mounted assembly. To provide a constant light distribution over the full image, three infrared light emitting diodes (LED) were mounted concentrically with the camera optics. The VOG signals were amplified before passing through a radio frequency transmission to a PC. These VOG signals were then processed (sample frequency = 50 Hz)

on the PC computer and stored both on the computer and a digital recorder for further off-line analysis.

### Paradigm

Full-field visual stimulation was induced by the displacement of the projected black and white dots pattern (constant velocity 50°/s) for a 90 s duration. The subject indicated the onset of the visual stimulation and of a self motion sensation by pressing a button of a chronometer held in the right hand. The ocular responses were recorded in the 3D planes (horizontal, vertical and torsional) during two successive phases: (1) a 90 s phase of visual stimulation as the optokinetic nystagmus (OKN) and (2) after the extinction of the visual stimulus, as a perseverative ocular responses or optokinetic after nystagmus (OKAN) for a 60 s period in the dark. The self-motion and the eye movements were investigated in four experiments characterized by visual full-field stimulation in presence of OKN or its absence due to gaze fixation at varying eccentricities and depth planes (Table 1). In Experiment 1, the effect of the visual stimulation was tested by horizontal motion of the visual pattern to the left, with gaze fixation (F0 condition) and without gaze fixation (NoF condition) forming 2 trials of 150 s each. In F0 condition, the subject had to fixate a visual target localized at the center of the screen and at the level of gaze line. In Experiment 2, we investigated the effect of the orientation of visual motion (to the left) in three successive sessions: (1) with the sphere rotating around the earth-vertical axis (0), providing an horizontal displacement of the visual pattern (2) with the sphere rotating around an axis now tilted 45° forward from the earth-vertical axis (45), providing an oblique displacement of the visual pattern and (3) with the sphere rotating around an horizontal axis orthogonal to the earth-vertical axis (90), providing a rotatory displacement of the visual field motion. Each orientation of the visual motion was studied in both F0 and NoF conditions as in Experiment 1. In Experiment 3, we investigated the effects of the direction (right and left) of the visual stimulus

motion in the horizontal plane at different eccentricities of gaze fixation. The NoF and F0 conditions were compared with 2 other conditions of gaze deviation (1) at 20° on the right (F20R) and (2) at 20° on the left (F20L) of the center of the screen. This Experiment 3 was thus realized in eight trials of 150 s each, NoF, F0, F20R and F20L in each right and left direction of the stimulus. In Experiment 4, we examined the effect of the depth plane of gaze fixation by comparing fixation of a center point localized at a near (50 cm) distance to the subject (Near condition tested in one trial of 150 s) versus a center point localized farther away (1 m) in the plane of the moving visual pattern (Far condition tested in one trial of 150 s).

The experiments were performed in a balanced order across the subjects. During the NoF the subject was instructed to gaze ahead and to avoid delineate fixation of any dots of the moving background. In the gaze fixation conditions, the subject was asked to fixate as much as possible the visual target independently of the moving background.

Prior to each test, a VOG calibration was performed on the horizontal and vertical saccades elicited with visual targets at 10° and 20° right and left, up and down.

### Data analysis

#### *Self-motion quantification*

At the end of each test, the subject had to describe his/her self motion sensation in terms of direction and orientation. The latency (Lat) of the self-motion occurrence was measured as the time elapsed between the onset of the visual stimulus and the onset of the sensation of self motion recorded by the chronometer.

#### *Eye velocity analysis*

Eye movements were analysed off-line by replaying the eye images from the digital tape. Using enhanced geometric and statistical filter methods, the image processor reconstructs the pupil center coordinates from a circular fit along the borders of the identified (thresholded) pupil area. The horizontal and vertical eye positions were measured on the position of the center of the pupil. The torsional position was derived from a circular ring segment selected on the iris. To evaluate torsional eye movements between two video images, the horizontal shift of the previously selected iris segment was analysed using a cross-correlation technique. Once the adequate parameters had been adjusted, the images were processed over several cycles and the 3D eye positions were extracted and stored on the computer. Finally the 3D eye position signals were analysed with an interactive software SAMO (Denise et al. 1996) that

**Table 1** Table summarizing the experimental conditions tested over the four experiments

	Conditions				
	No fixation OKN	Fixation			
		20R	20L	0 Far	0 Near
Experiment 1	NoF	–	–	F0	–
Experiment 2	NoF (3D)	–	–	F0 (3D)	–
Experiment 3	NoF	F20R	F20L	F0	–
Experiment 4	NoF	–	–	Far	Near

Gaze fixation at the centre (0), at 20° on the right (20R) and on the left (20L)

processed eye movement velocity by using the two-point central difference algorithm (50 ms step size). Quick phases were then removed by an algorithm using velocity and acceleration thresholds.

Three-dimensional eye movements were expressed in a head-centered coordinate system with the +X (roll) axis along the forward naso-occipital axis, the +Y (pitch) axis along the interaural axis to the left and the +Z (yaw) axis along the head vertical axis. Thus, the positive eye velocity and position values indicated, respectively clockwise, downwards and leftwards eye movements.

#### *Eye movement parameters*

Multiple parameters were quantified based on the nystagmus slow phase velocity (SPV) and position as follows:

The eye velocity was calculated (1) at the onset of the OKN response ( $V_p$  = averaged velocity of the two first slow phases included in the first 400–600 ms) reflecting the involvement of the direct pathway, i.e., the pursuit component and (2) at the steady state of OKN response ( $V_{okn}$ ) reflecting the involvement of the indirect pathway, i.e., the vestibular component. During the OKAN post-stimulus phase, the maximal slow phase velocity ( $V_{okan}$ ) was calculated immediately after the extinction of the visual stimulus (first beats); the OKAN time constant ( $TC_{okan}$ ) was measured on the progressive decline of the slow phases velocity curve as the time when the area under the slow phase velocity curve reaches 63% of the total area (Denise et al. 1996; Ventre-Dominey et al. 2008).

Finally, in Experiment 3, we measured the asymmetry of the ocular responses elicited when the visual pattern was moving to the right and to the left directions, using the following equation:  $As = (\text{right} - \text{left}) \times 100 / (\text{right} + \text{left})$ . Positive values indicate a right predominance and negative values a left predominance.

#### *Statistical analysis*

Based on the OKAN velocity analysis in the F0 condition, we distinguished two types of OKAN response (1) inverted OKAN (I OKAN) with slow phases directed away from the previous stimulus direction and (2) OKAN slow phases (NoI OKAN) directed to the stimulus direction. Based on these two types of OKAN responses obtained in F0 condition, we divided the OKAN responses into two Responses, not inverted (NoI) and inverted (I). A grouping analysis based on presence/absence of inversion was realized in an attempt to identify a possible mechanism for OKAN inversion, either due to velocity or time constant processing. A repeated measures ANOVA was performed on the dependent variables related to vection (Lat) and to eye movements ( $V_p$ ,  $V_{okn}$ ,  $V_{okan}$ ,  $TC_{okan}$  and  $As$ ). We analysed

the effects of the following within subject factors: in Experiment 1, the visual fixation conditions (F0 and NoF); in Experiment 2, the visual fixation conditions (F0 and NoF) and the stimulus orientations (0, 45 and 90); in Experiment 3, the direction of the visual pattern moving either towards (ipsilateral: F20ipsi) or away from (contralateral: F20contra) the visual fixation hemifield and in Experiment 4, the visual fixation conditions (Far, Near). In each experiment, the effects of the within-subjects factors on the different variables were compared between the two types of Responses (Response factors NoI and I). The vection and eye movement parameters were also compared by using the Pearson Product-Moment Correlation analysis. The statistical analysis was realized with STATISTICA software package. The significance level was established at a 95% confidence interval.

## **Results**

### Experiment 1: Effect of visual fixation

In all subjects ( $n = 23$ ), the visual full-field displacement induced in the NoF condition a strong OKN with slow phases directed toward the visual stimulus and averaged steady-state velocity of 31 deg/sec (SD  $\pm 7$ ). At the stimulus extinction, the OKN responses perseverated in the dark forming the so-called OKAN characterised by nystagmic slow phases (mean velocity: 7°/s, SD  $\pm 4$ ) in the same direction as both the OKN slow phases and visual field displacement (Table 2). A sensation of vection could be reported by the subject during the visual field displacement with or without visual fixation and this sensation was always directed in the direction opposite to the visual stimulus motion.

The major effect of the visual fixation F0 condition consists in inverted OKAN responses observed in the majority of subjects (65%). In these subjects, the visual fixation during full-field stimulation induced at the stimulus extinction an inversion of the OKAN characterised by nystagmic slow phases directed in the direction opposite to the visual stimulus (Table 2; Fig. 1). Because of these dual after nystagmus responses, we dissociated the OKAN responses into 2 Responses types: not inverted (NoI) and inverted (I) and compared the OKN and OKAN parameters between these 2 Responses types. As illustrated in Fig. 1, the inversion effect was thus quantified by a highly significant difference in the mean  $V_{okan}$  between the 2 OKAN Responses as expected during the F0 condition (main Response effect:  $F(1,21) = 16.2$ ,  $P < 0.001$ ) but also during the NoF condition (main Response effect:  $F(1,21) = 5.2$ ,  $P = 0.03$ ).

During the NoF condition, the mean OKN velocity tended to be slightly increased in subjects with I Response

**Table 2** Mean values of the ocular responses induced during visual field motion (50°/s to the left) in all subjects of Experiment 1

Cases	No fixation condition				Fixation condition			
	Vection latency (s)	OKN velocity (°/s)	OKAN velocity (°/s)	OKAN TC (s)	Vection latency (s)	OKAN velocity (°/s)	OKAN TC (s)	Response type
1	19	34.4	10.2	14	–	1	0.7	NoI
2	12	44	10.9	6.9	28	–9.1	24.6	I
3	20	29	8.7	17.5	–	–8.3	8.9	I
4	–	19	2	0.4	51	2.4	9.8	NoI
5	–	41.9	9.4	11.5	27	–3.8	10.6	I
6	26	11.6	5.9	0.8	15	1.5	1.9	NoI
7	25	38.3	5	6.3	29	0.9	1.2	NoI
8	22	35.4	5.1	2.1	14	–9.3	10.5	I
9	14	26.4	5.6	7.7	22	–1.2	14.2	I
10	11	35	6	8.9	6	–3.3	24.2	I
11	10	32.7	14.9	9.7	10.4	–1.1	0.7	I
12	18.5	28	9.1		–	–3.6	2.9	I
13	11.4	38.9	13.3	19.7	–	–1.3	0.6	I
14	33.3	24	4	5.9	25	–2.1	0.9	I
15	6.5	33	7.5	11.2	25	0.8	0.9	I
16	30	33	5	7.5	–	0.9	0.5	NoI
17	17	38.6	16.1	2.9	13	–6.1	31.6	I
18	–	29.9	1.7	1.5	–	1.7	4.8	NoI
19	–	28.1	5.9	6.5	–	1.2	1.8	NoI
20	12.2	30	5.2	2.7	–	–14	10	I
21	8.24	29.9	6.1	7.3	16.4	–2.7	10.9	I
22	8.5	26.8	2.6	3.4	3.6	–2.3	20.5	I
23	26	26.4	1.2	3.6	27.5	1.1	1	NoI
Means	25.2	27.6	4.6	5.0	30.6	1.3	2.8	NoI
	14.6	32.9	8.3	8.4	17.3	–4.5	11.5	I

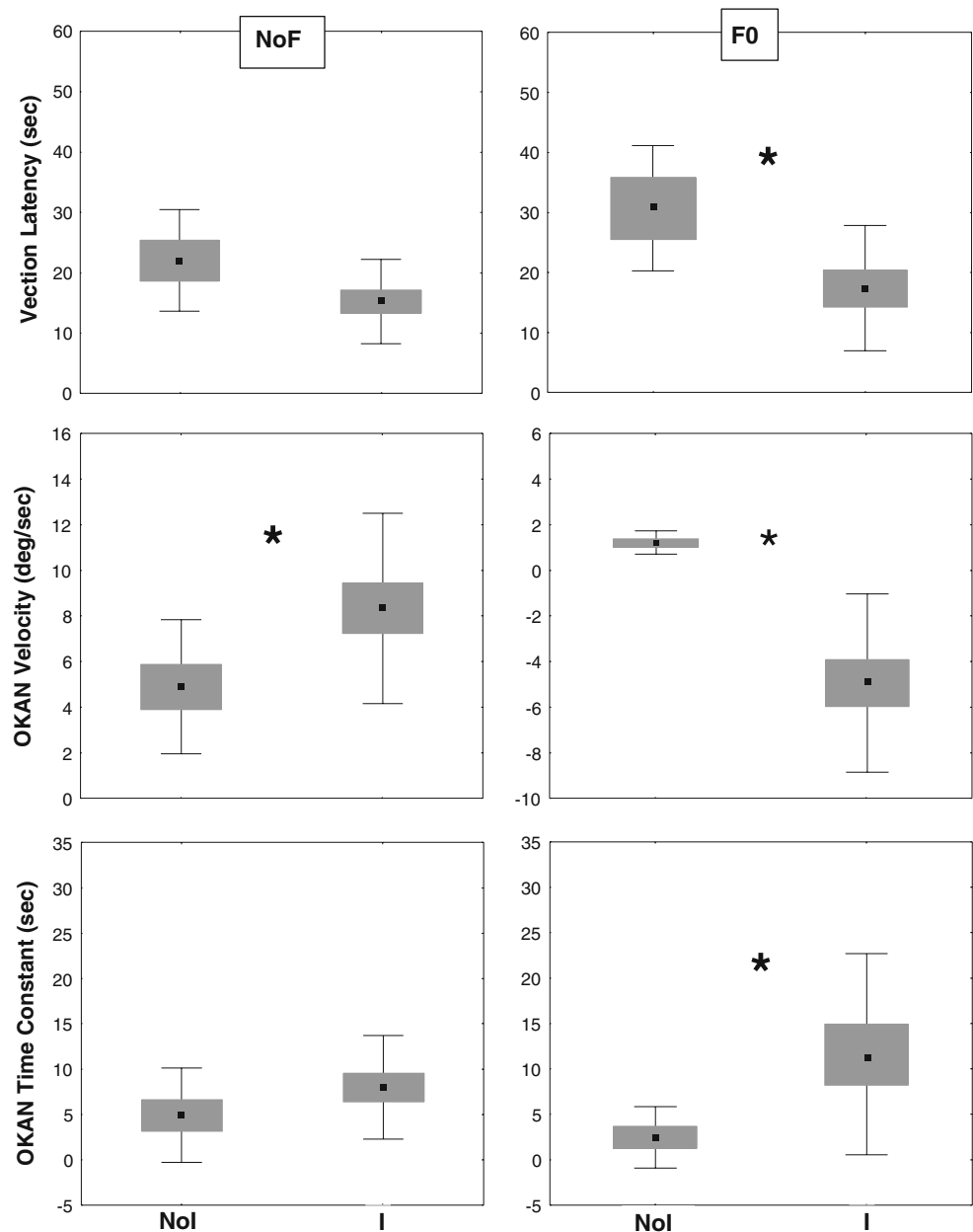
TC Time constant, *Response type* I indicates an inverted OKAN, *NoI* indicates OKAN slow phases in the same direction as the stimulus

Negative velocity values indicate inverted responses in fixation condition. Note that some subjects did not present any vection either in no fixation or in fixation condition

(33°/s; SD 6) as compared to those with NoI Response (28°/s; SD 9) (main Responses effect:  $F(1,21) = 3.02$ ,  $P = 0.096$ ). The pursuit component  $V_p$  measured at the onset of the OKN was not significantly different between the Response types (main Responses effect:  $F(1,21) = 0.09$ ,  $P > 0.05$ ). As shown in Fig. 1, the induced vection during the NoF visual stimulation significantly depended on the OKAN Response (main Responses effect:  $F(1,17) = 9.8$ ,  $P = 0.006$ ); the latency (Lat) for a self-motion sensation to occur was smaller in I (14.6 s; SD 7) as compared to NoI (25.2 s; SD 4) response. In NoF condition, the TCokan tended to be shortened in NoI as compared to I Response without reaching, however, the significance level (main Response effect:  $F(1,13) = 1.7$ ,  $P > 0.05$ ). While a correlation was found between TCokan and OKAN velocity only in NoI Response ( $r = 0.82$ ,  $P < 0.01$ ), no correlation was observed between Lat and both TCokan and OKAN velocity.

During F0 condition, a significant difference in vection latency was observed between the two Response factors NoI and I (main Response effect:  $F(1,13) = 4.8$ ,  $P = 0.047$ ) and, as in NoF condition, the self-motion susceptibility was larger in I Response (Fig. 1). Moreover, in NoF condition, 93% of the subjects with inverted OKAN versus 67% without inverted OKAN presented vection while in F0 condition, the number of subjects with vection decreased, respectively to 71 and 56%. The mean TCokan induced after fixation (F0) was highly related to the Response (main Response effect:  $F(1,21) = 9$ ,  $P = 0.007$ ). As illustrated in Fig. 1, in Response I the TCokan (12.7 s; SD = 10) was significantly greater than the TCokan in Response NoI (2.3 s; SD = 3.2). Furthermore, this latter TCokan tended to be smaller in the F0 condition (2.3 s; SD = 3.2) as compared to the NoF condition (4.9 s; SD = 2.7). As in NoF condition, OKAN velocity was significantly correlated to TCokan only during NoI Response ( $r = 0.95$ ,  $P < 0.001$ ).

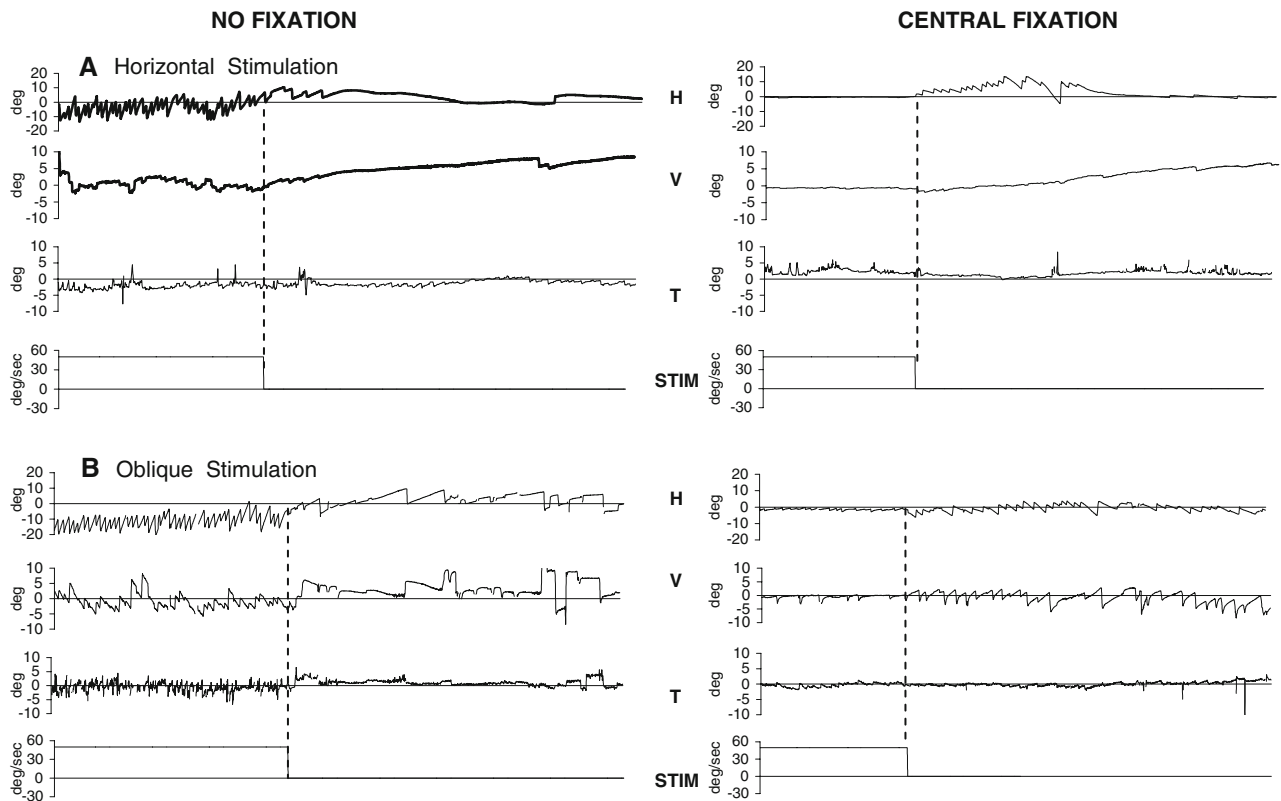
**Fig. 1** Mean values of vection latency, OKAN velocity and OKAN time constant with standard errors (*boxes*) and standard deviations (*whiskers*) for each Response type: with no OKAN inversion (*NoI*) and with OKAN inversion (*I*). The 2 columns represent the two conditions of Experiment 1: (1) no gaze fixation (*NoF*), (2) gaze fixation of a central visual target (*F0*).  
\* $P < 0.05$



#### Experiment 2: Effect of the visual stimulus orientation

The effect of the axis of visual motion orientation on OKAN inversion was investigated in the group of 14 normal subjects. A reversal OKAN could occur after OKN inhibition with different orientations of the visual pattern as well as in the different planes of the eye movements. For example as shown in Fig. 2, during the 45° tilted visual pattern, an OKAN inversion could be observed in the different planes of eye movements even though it is more frequent in the horizontal plane (post hoc  $P < 0.001$ ). As the axis of the visual moving pattern was increasingly tilted, the inversion phenomenon tended to diminish: 65% of the subjects presented an inverted OKAN during the

horizontal visual stimulation against 57% during the tilted (45° tilted axis) visual stimulation and 36% during circular (90° tilted axis) visual stimulation. Thus, with inverted OKAN, after gaze fixation with tilted visual stimulation, we observed for horizontal eye movements a significant Vokan decrease (main Group effect:  $F(1,10) = 17$ ,  $P = 0.0019$ ) and as in the previous experiment, a significant increase of TCokan (main Response effect:  $F(1,10) = 8.4$ ,  $P = 0.016$ ) (Supplementary Table). Interestingly, while the circular stimulus (90° orientation of the sphere's rotation axis) induced less inversion of the post-stimulus responses, this experimental condition could induce in some subjects an OKAN inversion both without and with gaze fixation.



**Fig. 2** Eye movement recordings showing OKAN inversion after OKN suppression (Central fixation) as compared to OKAN response after OKN release (No fixation) in the different ocular planes, horizontal (*H*), vertical (*V*) and torsional (*T*) as tested in Experiment 2. STIM: Motion of the visual background in the horizontal (**a**) and in the oblique (**b**) left direction. In No Fixation condition, the OKAN slow

phases are directed in the same direction as the OKN, i.e., in the direction of the visual stimulus. In Central Fixation condition: OKAN is inverted only in the horizontal plane during horizontal stimulation OKAN and in the three planes of eye movements during the oblique stimulation

### Experiment 3: Effect of the gaze fixation eccentricity

In nine subjects, we investigated the effects of the lateral deviation of gaze fixation by comparing OKAN induced during NoF, F0, F20R and F20L conditions in the 2 directions (right and left) of the visual pattern motion (Table 3). First, we could observe inverted OKAN in one direction and not in the other in some subjects (30%). The occurrence of the OKAN inversion observed during the F0 condition was significantly related to an asymmetry (*As*) of the TCokan obtained in NoF condition (main Response effect:  $F(1,10) = 5.1$ ,  $P = 0.04$ ). In condition of eccentric gaze fixation, we found that TCokan was strongly dependent on the direction of the stimulus and gaze deviation (Response  $\times$  Direction interaction:  $F(2,32) = 13$ ,  $P < 0.001$ ). As shown in Fig. 3, the TCokan was significantly shorter with a contralateral (away from gaze fixation) than with an ipsilateral (toward the gaze fixation) stimulus direction with Response I and the opposite with Response NoI obtained in F0 condition. The same pattern of TCokan dissociation was observed with less significance during NoI versus I Responses obtained in F20ipsi (Response  $\times$  Direction

interaction:  $F(2,30) = 2.8$ ,  $P = 0.08$ ) and F20contra (Response  $\times$  Direction interaction:  $F(2,3) = 4$ ,  $P = 0.03$ ) experimental conditions. As expected the Vokan was significantly lower in I as compared to NoI Response independently of the eye position (in F0, F20ipsi and F20contra) and of the stimulus direction in F0 condition (Response  $\times$  Direction interaction:  $F(2,32) = 1.8$ ,  $P > 0.05$ ). No effect of the lateral deviation of gaze fixation and of the stimulus direction was found in the vection Lat (Response  $\times$  Direction interaction:  $F(2,32) = 1$ ,  $P > 0.05$ ). We found a significant correlation between OKAN velocity and TCokan only in the experimental condition F20ipsi ( $r = 0.48$ ,  $P = 0.044$ ).

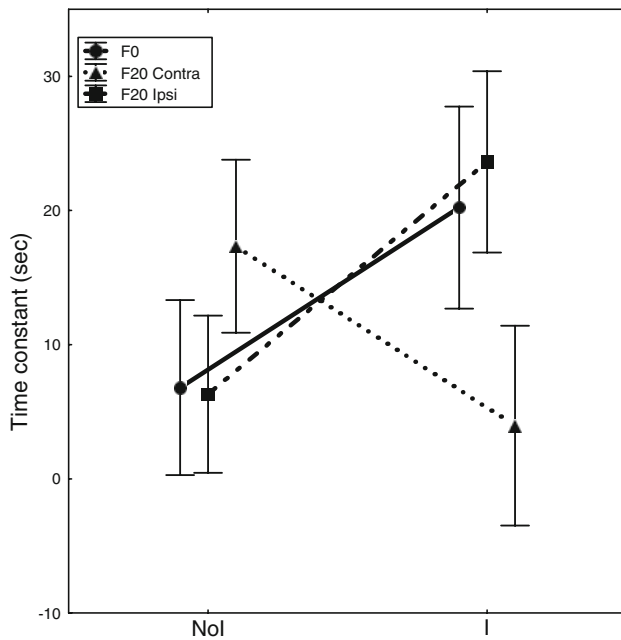
### Experiment 4: Effect of the far/near visual fixation

The effect of the depth plane of gaze fixation was examined in the same group of 9 subjects. The inversion of OKAN significantly diminished or even disappeared in some subjects in near condition as compared to Far condition (Table 4; Fig. 4). Thus, we distinguished two groups of OKAN Responses: I and NoI obtained after central fixation in the far space and after central fixation in the near space.

**Table 3** Mean values of the OKAN ocular responses induced after visual field motion ( $50^\circ/s$ ) to the right (R) and to the left (L) in all subjects of Experiment 3

Cases	Stimulus direction	Response type in F0	Response type in F20ipsi	Response type in F20contra	OKAN velocity ( $^\circ/s$ )			OKAN time constant (s)				
					NoF	F0	F20 Ipsilateral	F20 Contralateral	NoF	F0	F20 Ipsilateral	F20 Contralateral
1	R	I	I	NoI	6.80	-2.00	-2.20	0.80	2.6	29.10	31.50	8.10
	L	I	I	NoI	7.50	-0.80	-1.20	1.30	11.2	0.90	1.70	8.80
2	R	NoI	I	NoI	7.00	0.70	-1.30	1.90	10.3	5.00	9.60	34.80
	L	NoI	NoI	NoI	5.00	0.90	0.60	1.10	7.5	0.00	2.70	16.90
3	R	NoI	NoI	NoI	4.30	1.40	2.50	4.40	26	8.90	10.90	29.40
	L	I	I	NoI	16.10	-6.10	-5.90	0.70	2.9	18.20	27.70	4.10
4	R	NoI	NoI	NoI	5.20	1.20	1.70	1.40	5.3	25.50	14.00	21.80
	L	NoI	NoI	NoI	1.70	1.70	10.00	0.40	1.5	4.80	7.70	5.30
5	R	NoI	NoI	I	3.70	1.60	11.00	-1.40	5.3	3.00	1.50	1.90
	L	NoI	I	NoI	5.90	1.20	-1.50	2.40	6.5	1.80	1.90	5.00
6	R	I	NoI	I	13.90	-5.90	2.10	-1.20	16.5	19.20	7.50	4.30
	L	I	I	I	5.20	-13.70	-2.00	-10.80	2.7	10.00	36.60	3.80
7	R	NoI	NoI	NoI	10.30	2.50	4.00	3.70	9.5	2.70	3.00	15.00
	L	I	I	I	1.20	-2.70	-2.60	-2.90	7.3	10.90	19.10	1.00
8	R	NoI	NoI	NoI	6.50	3.30	2.50	3.80	13.4	6.60	3.30	4.30
	L	I	I	I	2.60	-2.30	-3.20	-2.70	3.4	20.50	19.30	2.50
9	R	NoI	NoI	NoI	7.40	0.90	1.20	1.10	13.8	2.10	3.50	3.60
	L	NoI	I	NoI	6.10	1.10	-3.10	1.30	3.6	1.00	2.00	2.20
Means		NoI			5.74	1.84	2.51	1.83	9.34	5.45	5.46	12.75
		I			7.95	-4.79	-1.38	-1.39	7.01	13.94	18.30	5.95
		NoI			6.44	0.84	3.96	1.48	10.98	8.09	6.01	11.39
		I			6.49	-2.73	-2.56	-0.89	5.61	10.82	16.60	7.81
		NoI		NoI	6.91	0.46	0.56	1.87	8.78	8.20	9.19	12.25
		I		I	5.32	-4.60	1.06	-3.80	7.04	12.72	16.80	2.70

*Response type* I indicates an inverted OKAN, *NoI* indicates OKAN slow phases in the same direction as the stimulus, *NoF* no fixation condition, *F0* fixation of a central target, *F20 Ipsilateral* fixation of a  $20^\circ$  visual target during a stimulus motion ipsilateral to the target side, *F20 Contralateral* fixation of a  $20^\circ$  visual target during a stimulus motion contralateral to the target side. Negative velocity values indicate inverted responses in fixation condition



**Fig. 3** Means and standard deviations of OKAN time constants showing the inter-group dissociation in the three conditions of fixation of Experiment 3: (F0) fixation of a central visual target, fixation of a 20° visual target located either in the visual field ipsilateral (F20ipsi) or contralateral (F20contra) to the direction of the background motion. NoI: Response with no OKAN inversion, I: Response with OKAN inversion

As shown in Table 4 and Fig. 4, in Near condition the differences between the two Response types previously described disappeared for all the parameters: Vokan (main Response effect:  $F(1,14) = 0.6$ ,  $P > 0.05$ ), TCokan (main Response effect:  $F(1,14) = 0.6$ ,  $P > 0.05$ ) and vection Lat (main Response effect:  $F(1,12) = 0.03$ ,  $P > 0.05$ ). In Near Condition some OKAN responses remained or became (for 1 subject) inverted. In these few cases (4 OKAN responses), while as expected the Vokan was significantly decreased during the Response I (main Response effect:  $F(1,14) = 26.7$ ,  $P < 0.001$ ), the TCokan did not significantly differ between the two types of Response I and NoI (main Response effect:  $F(1,14) = 0.25$ ,  $P > 0.05$ ). No significant correlation was observed between OKAN velocity and TCokan neither in Far nor in near condition ( $r < 0.5$ ,  $P > 0.05$ ).

## Discussion

This study investigates the characteristics of the after responses, OKAN obtained after OKN cancelation due to a gaze fixation during visual background motion. The eye movement inhibition during visual motion often yields, at the extinction of the stimulus, an inversion of the after responses in the different ocular planes. This OKAN inversion

phenomenon is dependent on the lateral deviation and the depth of the gaze fixation during the displacement of the visual field. In the following, we discuss these results in terms of possible extra-retinal mechanisms responsible for the reversal of the after responses following OKN inhibition.

### Velocity storage and inverted after-response

As traditionally described, whole visual field motion induces optokinetic nystagmus (OKN) with slow compensatory eye movements directed towards the visual motion (For review: Ilg 1997). These movements are maintained at the extinction of the visual stimulus, hence forming an after-response in the same direction as the OKN, the so-called optokinetic after nystagmus (OKAN). When the eye movements are inhibited by fixating a visual target localized at the centre of the moving visual field, we observe that the initial OKAN velocity is usually reduced and in the majority of subjects it is inverted, occurring with a direction of the slow movements opposite to the OKN movements. When the visual displacement was presented in the different planes of space, an inverted OKAN could be observed in the different planes of the ocular responses, horizontal as well as vertical and less frequently torsional. An OKAN inversion after eye movement inhibition was first reported by Brandt et al. (1974), and characterized in relation with a habituation process. Indeed, these authors interpreted the inversion of the OKAN direction occurring after long stimulus duration (15 mn) as the consequence of a central counter-regulation to a motion habituation acting upon vestibular nuclei. As we know, the OKN and OKAN result from a coupled activation of the direct visual (pursuit) and indirect vestibular (VSM) pathways, respectively, responsible for their initial velocity and the OKN steady-state and the OKAN duration (Cohen et al. 1977; Lafortune et al. 1986; Waespe and Schwartz 1986). The indirect pathway has been described as a velocity storage mechanism (VSM) responsible for the time constant of vestibulo-ocular responses as well as OKAN. In the current study, the OKAN time constant was significantly increased in the subjects presenting an inversion of the after-response as compared to the subjects with no inversion. Thus, in agreement with Brandt et al. (1974), we think that the vestibular nuclei are likely responsible for this OKAN reversal effect as being the main site of the VSM (Cheron et al. 1986; Katz et al. 1991; Cannon and Robinson 1987). In the subjects who did not present an OKAN inversion the reduction of the OKAN time constant evokes a dumping effect (reduction of the OKAN velocity) of the VSM due to visual fixation, as described by Waespe and Schwartz (1986). Similarly, Kudo et al. (2002) investigated the dynamics of the reversed OKAN in gaze fixation conditions and suggested an involvement of the velocity storage responsible

**Table 4** Mean values of the OKAN ocular responses induced after visual field motion (50°/s) to the right (R) and to the left (L) in all subjects of Experiment 4

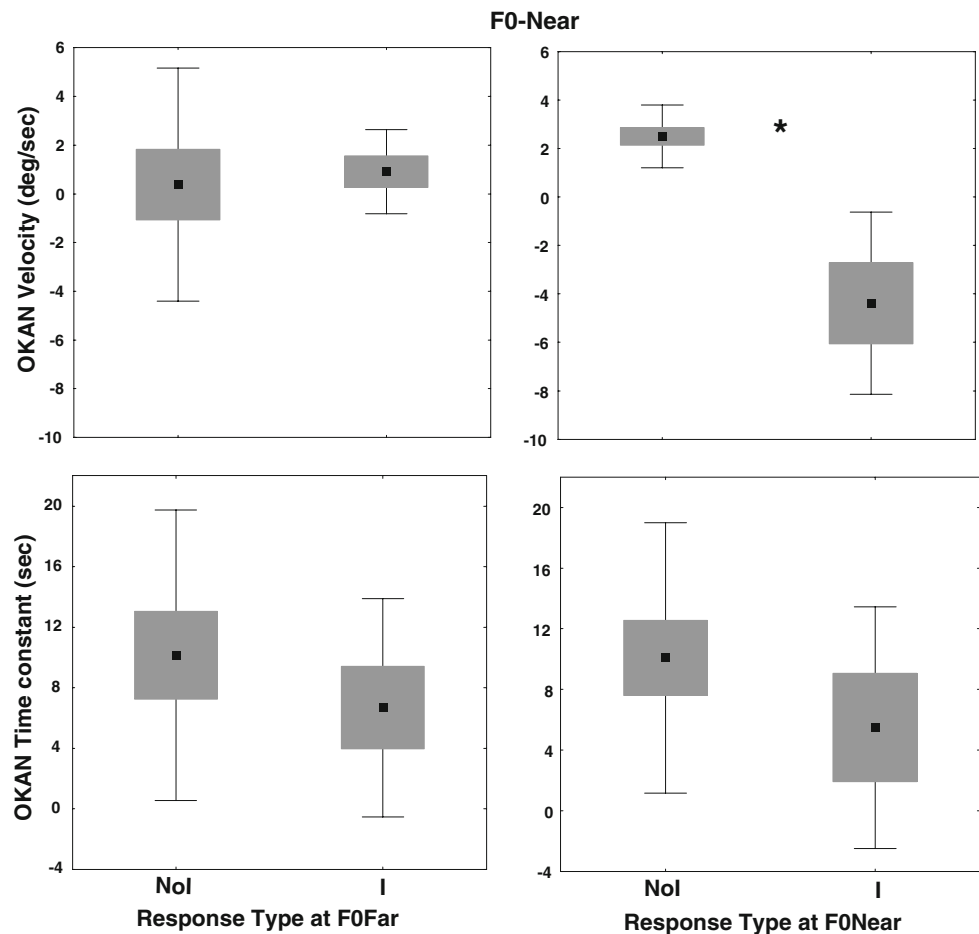
Cases	Stimulus direction	Response type in F0Far	Response type in F0Near	OKAN velocity (°/s)			OKAN time constant (s)		
				NoF	F0 Far	F0 Near	NoF	F0 Far	F0 Near
1	R	I	I	6.80	−2.00	−1.60	2.60	29.10	19.50
	L	I	NoI	7.50	−0.80	1.40	11.20	0.90	5.20
2	R	NoI	NoI	7.00	0.70	0.60	10.30	5.00	8.50
	L	NoI	NoI	5.00	0.90	3.20	7.50	0.00	30.40
3	R	NoI	NoI	4.30	1.40	4.30	26	8.90	19.30
	L	I	I	16.10	−6.10	−1.50	2.90	18.20	1.10
4	R	NoI	NoI	5.20	1.20	1.60	5.30	25.50	20.70
	L	NoI	NoI	1.70	1.70	2.10	1.50	4.80	3.10
5	R	NoI	NoI	3.70	1.60	1.40	5.30	3	3.70
	L	NoI	NoI	5.90	1.20	0.50	6.50	1.80	2.20
6	R	I	NoI	13.90	−5.90	2.30	16.50	19.20	14.10
	L	I	NoI	5.20	−13.70	1.80	2.70	10.00	1.30
7	R	NoI	NoI	10.30	2.50	3.80	9.50	2.70	13.00
	L	I	NoI	1.20	−2.70	1.50	7.30	10.90	2.70
8	R	NoI	NoI	6.50	3.30	2.20	13.40	6.60	6.60
	L	I	NoI	2.60	−2.30	2.50	3.40	20.50	2.90
9	R	NoI	I	7.40	0.90	−2.00	13.80	2.10	0.90
	L	NoI	I	6.10	1.10	−9.50	3.60	1.00	4.50
Mean		NoI		5.74	1.50	0.75	9.34	5.58	10.26
		I		7.61	−4.79	0.91	6.66	15.54	6.69
			NoI	5.71	−0.78	2.09	9.03	8.56	9.55
			I	9.10	−1.53	−3.65	5.73	12.60	6.50

*Response direction* I indicates an inverted OKAN, *NOI* indicates OKAN slow phases in the same direction as the stimulus, *NoF* no fixation condition, *F0 Far* fixation of a central target situated in the far space (background), *F0 Near* fixation of a central target situated in the near space. Negative velocity values indicate inverted responses in fixation condition.

for this OKAN. These authors in agreement with Brandt et al. (1974) suggested that the OKAN inversion can be related to a motion habituation process involving the VSM. In our study, self-motion perception built up more quickly in conditions of OKAN inversion suggesting a greater susceptibility to visual motion and consequently a possible perceptive habituation related to OKAN inversion. In agreement with this assumption, in conditions when the visual motion triggered OKAN reversal, the time constant of the inverted OKAN increased as well as the OKN velocity induced with the same visual motion direction and thus independently of the motor responses direction (opposite between OKN and inverted OKAN). As concerns the habituation involvement in OKAN inversion, these observations are suggestive of a role of a perceptual component of habituation mechanisms likely due to a greater susceptibility for global motion. However, perceptual habituation mechanisms cannot account for all of our findings, particularly those of Experiment 3 related to lateral gaze fixation, and alternative hypotheses including extra-retinal influences must be taken into consideration.

As a whole, the visual fixation during full-field motion induced either a dumping effect of the OKAN response or an inversion of this after response, both reflecting inhibitory action on the visuo-vestibular system, including VSM. Likewise, evidence has been provided that OKN cancellation observed during visual fixation could be due to inhibitory extra-retinal signals coming from the smooth pursuit eye movements (Pola et al. 1995; Lindner and Ilg 2006). Moreover, recent neuro-imaging studies have revealed large overlapping neural networks involved in smooth pursuit and fixation suppression of OKN in human (Dieterich et al. 1998; Bense et al. 2006; Schraa-Tam et al. 2008). Based on these observations and our data, the smooth pursuit or gaze holding system might contribute to eye movement cancellation during visual background motion by sending inhibitory signals onto the vestibular nuclei (VSM) on one side which by push-pull activity, would concurrently release the contralateral inhibition. Therefore, after OKN inhibition, the after responses including OKAN dumping and reversal, would result from such an inhibition pattern into the vestibular nuclei complex. In this context,

**Fig. 4** Mean values of OKAN velocity and OKAN time constant with standard errors (boxes) and standard deviations (whiskers) obtained in Experiment 4 with gaze fixation of a central visual target located in near space (F0-Near) for each Response type: with no OKAN inversion (NoI) and with OKAN inversion (I). \* $P < 0.05$



we hypothesized that the OKAN reversal might also be linked to the coupling between inhibitory influence from the pursuit system and imbalance in the vestibular nuclei, i.e., the VSM, detectable by OKAN time constant asymmetry. In order to further investigate this assumption, the OKAN responses were compared in the two directions of the visual background motion during free OKN as well as OKN inhibition conditions. Indeed, we found that the occurrence of an OKAN reversal after eye movement cancellation was related to asymmetrical OKAN observed after OKN release. As expected, the direction of the visual field motion that induced OKN followed by weak OKAN responses subsequently induced reversed OKAN after OKN suppression. Thus we postulate that the OKAN reversal could be linked to an extra-retinal inhibition combined with an asymmetrical activity in the VSM vestibular complex.

When fixating eccentric targets, the sustained effort due to the gaze deviation is similar to an intentional pursuit command in the same direction as the gaze deviation (Heckmann et al. 1991). This pursuit signal is registered in the perceptual system and can affect the circular vection and likely the after response (Heckmann et al. 1991;

Nakamura and Shimojo 2003). Indeed, Nakamura and Shimojo (2003) showed that gaze deviation influences the strength of vection depending on the direction of the deviation. Likewise, in our study, when there was no OKAN inversion, the OKAN response was significantly more pronounced (greater time constant) when the visual stimulus was moving away from the side of gaze fixation. In contrast, the opposite pattern was found in case of OKAN inversion, i.e., a prolonged OKAN response (greater time constant) was observed when the visual stimulus was moving to the side of gaze fixation. This double dissociation in OKAN time constants is suggestive of an imbalance effect of eye position onto the VSM processing that is diverging between the cases with versus without OKAN inversion. Indeed, when the visual field is moving against the gaze deviation, the eye-position-related tonic activity is opposite to the OKN command, generating slow eye movement towards the visual stimulus. In consequence, the inhibitory signals driven by the smooth pursuit system to oppose the slow OKN component are released reducing thus the effects of gaze fixation, i.e., OKAN dumping and reversal. In contrast, when the visual field is moving towards the gaze deviation, the eye position related tonic activity is combined

with the OKN command and the inhibitory actions are maintained or even reinforced to keep the eyes from moving towards the stimulus. In agreement with Lindner and Ilg (2006), these results argue in favor of an extraretinal influence in relation to the dynamics of the vestibulo-motor system, rather than for a purely perceptual influence on the inverted OKAN mechanisms.

Based on our results and those of the literature, we think that the after response generation, including OKAN reversal induced after visual motion implies perceptual habituation as previously described but also extra-retinal mechanisms linked to the vestibular and pursuit motor systems.

#### Cognitive aspects and inverted after-response

Finally, when the subjects were asked to fixate a central visual target in their near space, the inversion of OKAN response tended to decrease or disappear in several subjects. Such a distance related effect of the fixation target on OKAN occurrence can rely on a visual/cognitive assumption that a near visual fixation might trigger direct visual pathways of the visual system partially bypassing the VSM in the vestibular nuclei. The weak OKAN response observed after a near target fixation might be the result of residual activity of the vestibular nuclei due to the background motion. We suggest a depth-weighted interaction between the attentional/pursuit and the vestibular systems with a predominant attentional/pursuit influence when the visual target fixation is in the near space and the opposite when the visual fixation is far, included in the moving visual background. Studies on perceptual effects of optokinetic stimulation have shown that vection induced by visual field displacement is dominated by more distant and/or not attended visual motions as compared to nearer and attended visual motion (Ohmi and Howard 1988; Telford et al. 1992; Kitazaki and Sato 2003). Kitazaki and Sato (2003) concluded that motion arising from the environment (ground) induces self motion sensation while motion arising in near space from objects does not. Likewise, evidence has been provided for a dichotomy of the optokinetic system organisation: (1) one relates to the direct path linked to smooth pursuit; this sub-system would be at the origin of the initial rise of the OKN velocity and of the look OKN induced by actively tracking the moving details in the visual field and (2) a second sub-system relates to the indirect path linked to the vestibular mechanisms (VSM); this sub-system would be at the origin of the secondary steady-state of the OKN response, its prolonged after response (OKAN) and the stare nystagmus resulting from reflexive eye tracking of the whole moving visual pattern without looking at specific details (Ilg 1997, for review). While the indirect visuo-vestibular system might be involved in slow dynamics and self

motion perception related to non-attended background motion, the direct pursuit related system might be involved in attended visual feature moving in near space. Howard's work (Howard and Gonzalez 1987; Howard and Simpson 1989) demonstrates that OKN production depends on the stereopsis system, as OKN is reduced when the moving stimulus is displayed with horizontal binocular disparities. When fixating a near visual target, the moving background is viewed with disparate visual features and is less reliable to trigger OKN and OKAN indirect responses. Based on these observations and our results, it is possible that the gaze fixation of a near visual target during a background motion triggers the direct visual system related to attention/pursuit system with less contribution of the indirect path including the VSM.

In conclusion, this study investigated through 4 experiments the possible mechanisms at the origin of the OKAN inversion observed after eye movement inhibition due to gaze fixation. Our main results suggest that the reversal of OKAN could be linked to inhibitory extra-retinal signals combined with asymmetrical activity in the VSM vestibular complex. The effect of the visual target distance on the OKAN pattern is likely linked to the dichotomic organisation of the optokinetic system. The gaze fixation of a near visual target during a background motion might trigger the direct visual system related to attention/pursuit system with less contribution of the indirect path including the VSM generating OKN and OKAN responses. Finally, we argue in favor of an extra-retinal influence in relation to the dynamics of the vestibulo-motor system, rather than to a purely perceptual origin of the inverted OKAN mechanisms.

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