

# Total sleep deprivation can increase vestibulo-ocular responses

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**SUMMARY** The effect of sleep deprivation on the vestibular function is largely unknown. Some studies have found that postural balance or vestibular reflexes are decreased in sleep-deprived subjects while others found no change. The aim of this study was to evaluate the effect of sleep deprivation on the vestibulo-ocular reflex (VOR). Horizontal eye movements were recorded in healthy subjects during earth vertical axis rotation in darkness once after an ordinary night sleep and once after 26–29 h of sleep deprivation. In the first experiment ( $n = 8$ ), for which rotation was a  $60^\circ \text{ s}^{-1}$  velocity step, sleep deprivation induced a significant increase in VOR gain. In the second experiment ( $n = 12$ ), for which rotation was sinusoidal ( $0.2 \text{ Hz} \pm 25^\circ \text{ s}^{-1}$ ), sleep deprivation induced no significant modification in VOR gain. The difference between the two studies was the abrupt onset of the step stimulation in comparison with the sinusoidal rotation. Because of its unexpected onset and the potential threat to postural balance, the step stimulation may activate the system specialized in reorienting attention towards salient or behaviourally relevant events. This system includes the right temporoparietal cortex, an area also involved in VOR control. A number of studies have found that sleep deprivation alters the activity of this cortical area during attentional tasks. It is therefore our hypothesis that the difference between the effects of these two vestibular stimulations results from a sleep deprivation-induced modulation of the right temporoparietal cortex.

**KEYWORDS** attention, eye movements, sleep deprivation, vestibulo-ocular reflex

## INTRODUCTION

The vestibular apparatus is composed of semicircular canals and otolith organs which detect angular and linear acceleration of the head respectively. The afferent vestibular activity combined with visual and somatosensory inputs is used to maintain a stable representation of space during change in body position or motion. In this context, any vestibular malfunctioning can result in a misperception of the body position or movements relative to external space. The effects of sleep deprivation on vestibular responses have been the subject of a very few studies. If sleep deprivation induces impairments in vestibular function, we can expect repercussions on postural balance, driving, piloting aircraft, etc.

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We know that sleep deprivation alters daytime cognitive and psychomotor functioning (review in Bonnet, 2002), including increased sleepiness or reduced alertness and alterations of more localized cortical function (Wu *et al.*, 1991; Horne, 1993; Drummond *et al.*, 2000, 2001; Thomas *et al.*, 2000; Drummond and Brown, 2001). Especially, it has been shown that sleep deprivation in humans can induce an alteration in the posterior parietal cortex (Drummond and Brown, 2001) that plays a crucial role in the processing of vestibular information in relation with space representation.

Anatomical studies provide evidence in primates of direct reciprocal connections between the vestibular nuclei and a number of vestibular-related cortical areas extending from the posterior parietal cortex to the frontal regions (Ventre and Faugier-Grimaud, 1988; Akbarian *et al.*, 1993; Fukushima, 1997). The parietotemporal and the retroinsular cortices (PIVC) receive projections from vestibular nuclei and are activated during vestibular stimulation in monkey (Guldin and Grusser, 1998). Using unilateral cortical lesions, it has been

shown that the parietotemporal cortex exerts a direct control on the symmetry of the vestibulo-ocular function in monkeys (Ventre and Faugier-Grimaud, 1986). With neuroimaging techniques, it has been shown in man that experimental stimulation of the vestibular system such as caloric stimulation (Bottini *et al.*, 2001; Suzuki *et al.*, 2001) or galvanic stimulation (Bucher *et al.*, 1998; Lobel *et al.*, 1998, 1999; Bense *et al.*, 2001) activates the multisensory parietoinsular cortex, the human homologue of the PIVC. More recently, Petit and Beauchamp (2003) demonstrated that head movement producing stimulation of the vestibular system is accompanied by activation of cortical areas including the posterior part of the planum temporale and the cortex at the temporoparietal junction (TPJ). From a functional point of view, lesion in the TPJ causes a misperception of verticality (Brandt and Dieterich, 1994) and asymmetrical disturbances of vestibulo-ocular reflex (VOR) (Ventre-Dominey *et al.*, 2003). Taken together, these observations are suggestive of a cortical influence originating from the parietotemporal cortex on the vestibular function.

As this cortical region can be functionally modified after sleep deprivation, we hypothesize that sleep-deprived subjects might also display changes in their vestibulo-ocular performance.

A few studies focus on the effect of sleep deprivation on the vestibular function. Some studies concern posturographic measurements after sleep loss: Uimonen *et al.* (1994) showed that postural stability did not deteriorate after 24 h of sleep loss. Schlesinger *et al.* (1998) found that while postural sway was not changed in response to the only sleep deprivation, it increased when a secondary information processing task was associated. With regard to the vestibulo-ocular response, only two studies so far have described the effects of sleep loss on the VOR performance. First, Wolfe and Brown (1968) found no significant difference in VOR after 25–28 h of sleep deprivation. Collins (1988) reported that the VOR velocity and duration remained unchanged after 24 h of sleep deprivation and decreased from 48 to 52 h of sleep deprivation. These behavioural studies are providing poor information on the effects of sleep deprivation on the different aspects of vestibular function.

The aim of our study was to provide a better insight into the consequence of short total sleep deprivation (26–29 h) on the vestibulo-ocular reflex and more specifically on the canal-ocular responses.

For this purpose, subjects performed a rotatory test for evaluation of the canal-ocular function after a night of normal sleep and after 26–29 h sleep deprivation. The test was either a velocity step or a sinusoidal rotation.

## MATERIAL AND METHODS

### Subjects

We studied 20 healthy volunteers (mean age  $21.1 \pm 1.4$  years). All subjects gave their informed consent to participate in the study, which was approved by the local ethics committee.

### Recording of horizontal eye movements

A sequence of horizontal eye movements calibration was applied systematically before each test. Horizontal eye movements were recorded by electro-nystagmography for the sinusoidal rotation experiment and by an infrared light reflection eye-tracking system (Iris, Skalar, the Netherlands) for the velocity step experiment. Eye position was sampled on-line at 100 Hz and eye velocity was calculated digitally using the two-point central difference algorithm (50 ms step size). Quick phases were then removed by an algorithm using velocity and acceleration thresholds, then systematically checked and corrected manually as required (Denise *et al.*, 1996).

### Sleep deprivation

Each subject performed the vestibular test once after a standard night and once after a 26- to 29-h sleep deprivation. A 2-week interval separated the vestibular tests, with half the subjects starting with the sleep deprivation and the other half with the control night. Subjects were studied in five groups of four each. They arrived for the experiment at 17:30 hours. A standardized meal was taken at 19:00 hours. Then two subjects (previously randomly selected) stayed in the laboratory while the two others went back home to sleep after they were asked to wear an actigraph to monitor their sleep duration. The subjects slept at home for the control nights because we wanted them to sleep as well as possible with no disturbances due to a different bed, noise, environment, etc. As the subjects were young and good sleepers, an actigraphic control of the night was appropriate: it has been shown that wrist actigraphy is a good indicator of sleep and wakefulness and is strongly correlated to polysomnography (Horne *et al.*, 1994; Tryon, 2004). Analysis of their actimetric profiles showed that all the subjects had normal sleep. During the night, they were not allowed to smoke, eat or drink anything except water. At 7:30 hours the following morning, the two subjects who had slept at home returned to the laboratory and the four subjects had breakfast. The experiment was then conducted between 10:00 hours and 12:30 hours.

### Vestibular stimulations

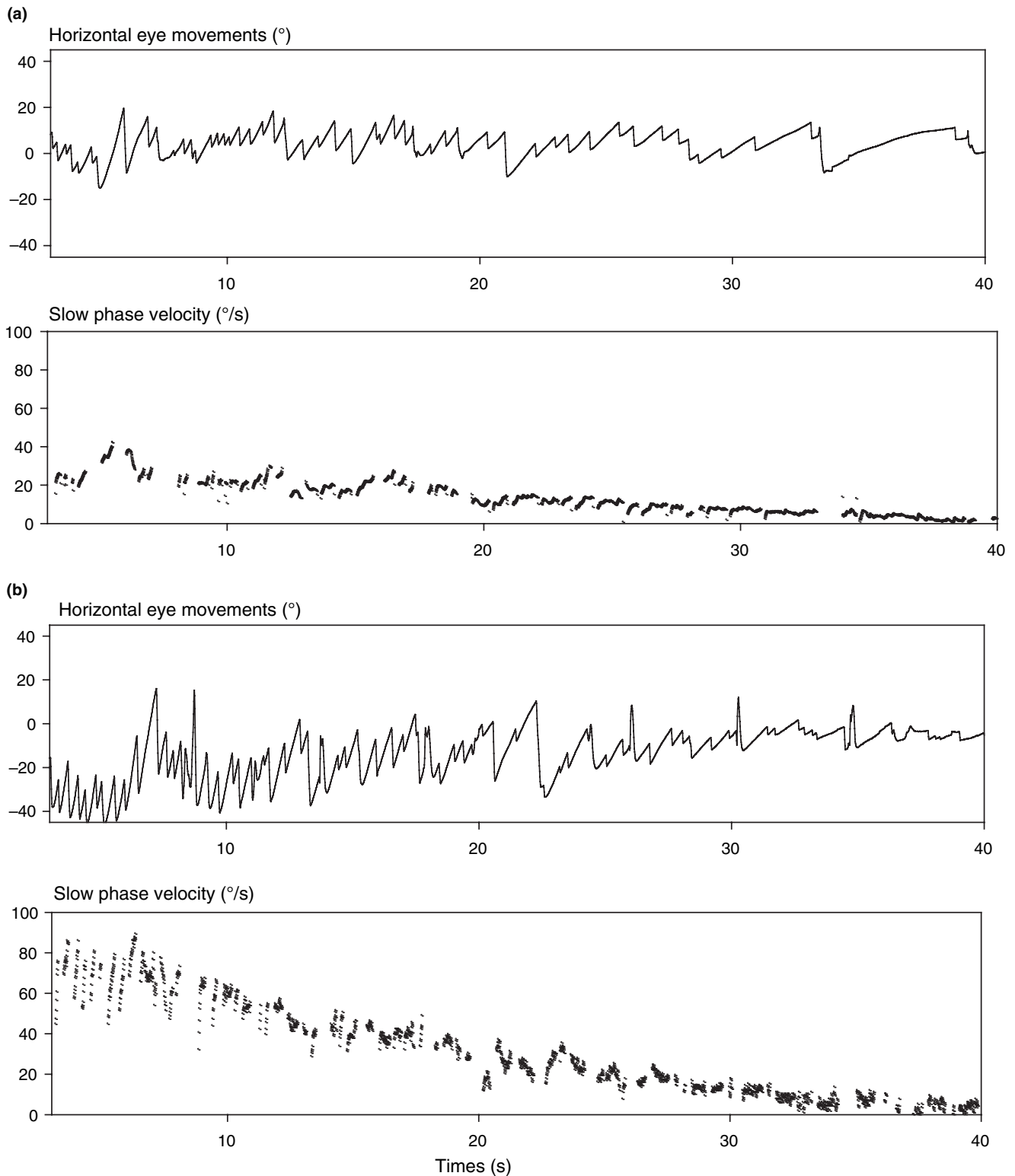
The VOR was evaluated using a rotatory chair. Subjects were seated with their heads upright and restrained. All testing was performed in darkness with eyes open.

In the first experiment ( $n = 8$ ), the subjects were rotated with a velocity step from 0 to  $60^\circ \text{ s}^{-1}$  (angular acceleration  $100^\circ \text{ s}^{-2}$ ) in the two directions (clockwise and counterclockwise). The constant velocity ( $60^\circ \text{ s}^{-1}$ ) rotation lasted for 90 s (prerotatory nystagmus) and stopped in 0.6 s (angular deceleration  $100^\circ \text{ s}^{-2}$ , postrotatory phase). Half the subjects began with clockwise rotation and the other half with counterclockwise. Acceleration and deceleration of the chair stimulate the semicircular canals, causing a nystagmus to appear (canal-ocular reflex) with slow compensatory phases, i.e. in the opposite direction to the chair rotation, alternating with rapid

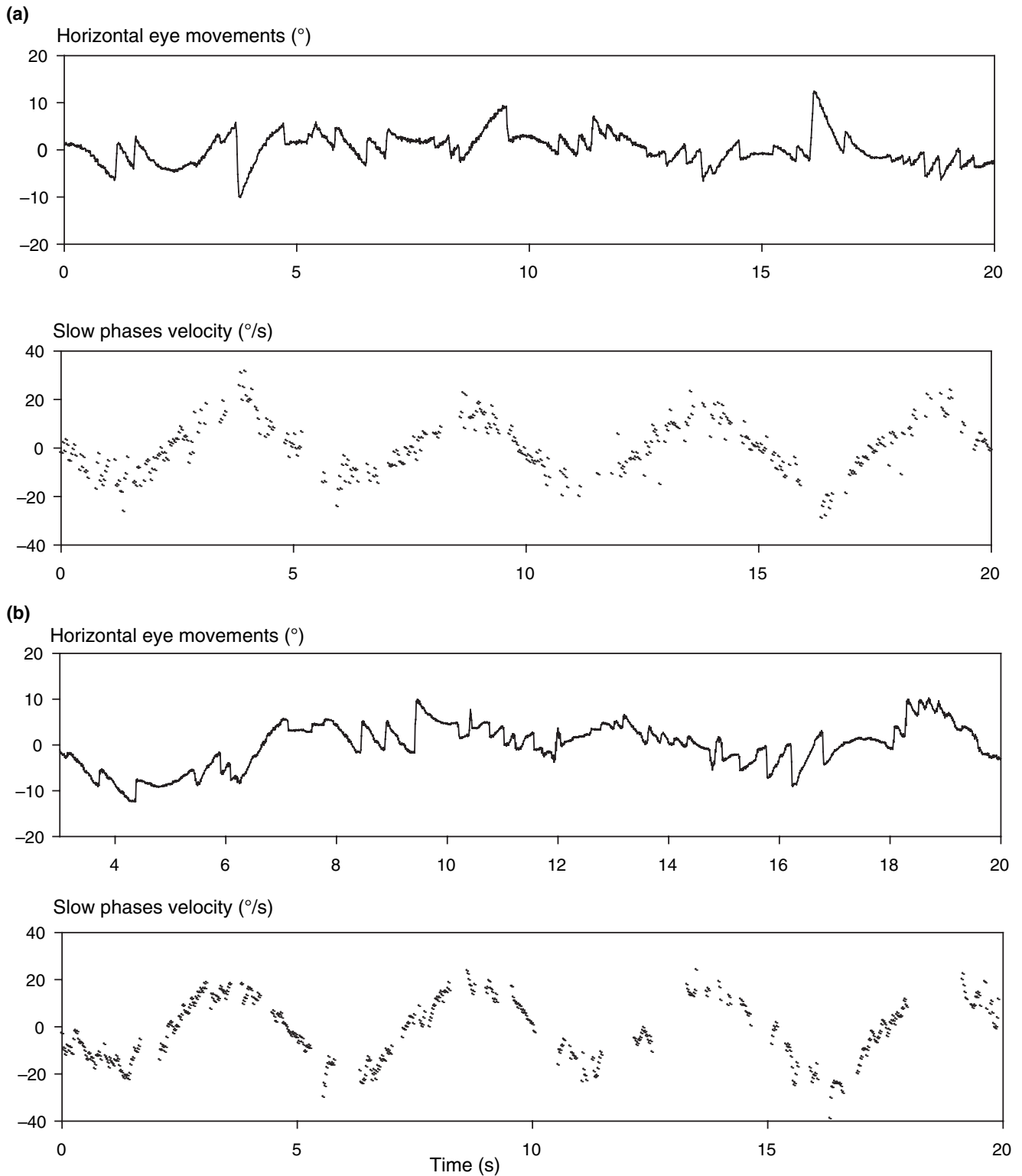
anticompensatory phases. The slow phase velocity of nystagmus decreases exponentially over time (see Fig. 1).

In a second experiment ( $n = 12$ ), the subjects were sinusoidally rotated for 50 s with a velocity amplitude of  $\pm 25^\circ \text{ s}^{-1}$

and a frequency of 0.2 Hz (maximum chair acceleration was  $0.32^\circ \text{ s}^{-2}$ ). As shown in Fig. 2, compensatory eye movement velocity is sinusoidal.



**Figure 1.** Example of horizontal eye movement recordings during a counterclockwise velocity step ( $60^\circ \text{ s}^{-1}$ ) for one subject in two conditions: (a) after one night of normal sleep or (b) after one night of sleep deprivation.



**Figure 2.** Example of horizontal eye movement recordings during a sinusoidal stimulation for one subject in two conditions: (a) after one night of normal sleep or (b) after one night of sleep deprivation.

**Data analysis**

Slow-phase eye velocity was analysed and the following parameters were extracted: (i) velocity step response: gain

(eye maximal velocity/head velocity) and time constant of the exponential decrease of slow phase velocity. Perrotatory and postrotatory parameters were averaged because they were not significantly different (paired *t*-test). (ii) Sinusoidal rotation:

gain (eye velocity amplitude/head velocity) and phase (angular difference between maximal slow phase velocity and maximal chair rotation velocity). We used a paired *t*-test to compare the parameters in the two conditions (sleep deprivation and normal sleep).

## RESULTS

### Velocity step test

Fig. 1 represents a typical VOR for one subject after normal sleep and after sleep deprivation. It is interesting to note that after sleep deprivation, the slow phases of the nystagmus were sharper (b, upper trace) and the maximum slow-phase velocity was higher (b, lower trace), while the duration of the nystagmus remained unchanged at a value of about 40 s.

By analysing the whole population, the mean gain (Fig. 3a) was significantly lower after a normal night's sleep ( $0.77 \pm 0.16$ ) than after total sleep deprivation ( $0.90 \pm 0.18$ ) ( $P < 0.005$ ). No effect of sleep deprivation was found on the time constant ( $12.3 \pm 2.84$  s in control condition versus

$11.8 \pm 2.60$  s in sleep loss condition). These results show that total sleep deprivation increases VOR magnitude observed after the velocity step, but not its duration.

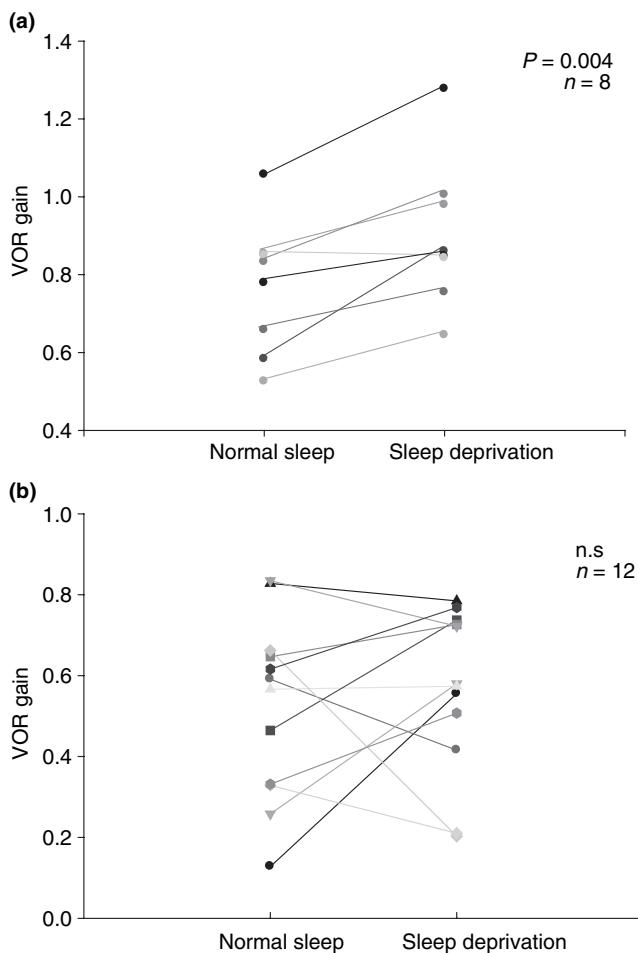
### Sinusoidal rotation test

There was no difference in gain or phase (Figs 2 and 3b) evaluated after a control night or after sleep deprivation (mean gain was  $0.55 \pm 0.22$  versus  $0.57 \pm 0.20$ , mean phase was  $185.8^\circ \pm 16.2^\circ$  versus  $184.2^\circ \pm 19^\circ$ ).

## DISCUSSION

Our main finding is that sleep-deprived subjects displayed an increased slow-phase eye velocity of the VOR elicited by a velocity step and not by sinusoidal rotation. We must consider that the paradigm we have chosen, the control night spent at home, has induced several differences between the control and the sleep-deprived conditions. The first difference is obviously the sleep duration: this is the key point of the study as we set out to compare subjects in normal sleep condition with subjects in sleep-deprived condition. But, as some environmental factors (temperature, hydration during the night, travel between home and the lab) could have been different at home and in the laboratory, this paradigm could also have induced non-sleep-related differences between the two conditions. However, none of these environmental factors is known to alter vestibular functions. Moreover, differences in environmental factors were minimal. Apart from water, subjects ate nothing during the night and all meals before and after sleep or sleep deprivation (dinner and breakfast) were standardized meals. All the subjects lived near the laboratory (less than 10 min by car), so there was no travel fatigue. As the experiment was performed in a temperate country, climatic and environmental variations between conditions were minimal. All subjects, with or without sleep deprivation, met up for breakfast at 7:30 hours while the experiment did not start until 10:00 hours, leaving a 2.5 h interval during which any effects that might have existed due to travelling in or different hydration levels had probably disappeared. One final argument is that in test-retest studies VOR parameters are remarkably stable and thus only marginally influenced by environmental factors. For example, Collins (1988) found no variation in VOR parameters of control subjects in five consecutive sessions spread over 3 days. Thus, our finding that sleep deprived subjects displayed an increased velocity step VOR and an unchanged sinusoidal VOR can be confidently attributed to sleep deprivation.

Previous studies found no modification of the VOR after a period of sleep deprivation comparable to ours (1 day) (Wolfe and Brown, 1968; Collins, 1988). The type of vestibular stimulation could explain this discrepancy. In the two earlier studies, the vestibular stimulation was based on a slow dynamic trapezoidal rotation, i.e. with a much longer and much less intense acceleration phase than the velocity step used here:  $5^\circ \text{ s}^{-2}$  for 18 s for Collins and  $20^\circ \text{ s}^{-2}$  for 10 s for Wolfe



**Figure 3.** Vertical point plots of individual vestibulo-ocular responses (VOR) gain in conditions of normal sleep and sleep deprivation during a velocity step test (a) and during a sinusoidal rotation test (b).

and Brown, as compared with the  $100^\circ \text{ s}^{-2}$  for 0.6 s used in our study. Likewise, the sinusoidal stimulation we used also involves low acceleration over a long period ( $0.32^\circ \text{ s}^{-2}$  for 50 s). Also, in comparison with sinusoidal stimulation, the onset of velocity step occurs unpredictably. It would therefore appear that after sleep deprivation, an increased VOR gain is only observed when vestibular stimulation is impulsive, i.e. intense and of short duration. In everyday life situation, such stimulation would threaten postural stability.

It is well known that unfamiliar sudden or distinctive stimuli can grab our attention (see review in Corbetta and Shulman, 2002). This attention-grabbing effect was described early on (James, 1890) and has subsequently been the subject of many studies, often examining the response to infrequent target, non-target or novel non-target deviant stimuli embedded in a repetitive train of standard stimuli. Functional imagery studies have shown that the prefrontal cortex and also the TPJ and hippocampus play a role in detecting novel or salient stimuli. Some of them have shown that the TPJ cortex seems to be particularly involved in reorienting behaviour to an unexpected stimulus: Knight and Scabini (1998) showed that TPJ damage reduces the amplitude of P300 scalp electrical potentials, which are commonly elicited by the detection of infrequent visual, auditory and somatosensory targets. More recently, using event-related functional magnetic resonance imaging, Corbetta *et al.* (2000) showed that cortical activation occurred in the right TPJ when the target was detected, particularly at an unexpected location. Interestingly, this region is known to be involved in the control of vestibular reflexes: Ventre-Dominey *et al.* (2003) observed that unilateral cortical lesion of the TPJ cortex in patients induced VOR gain and time constant asymmetry. Finally, functional imaging found that TPJ activity during attentional tasks was altered by sleep deprivation (Drummond and Brown, 2001; Drummond *et al.*, 2001).

We, therefore, hypothesize that our results may be explained by a sleep deprivation-induced modulation of this TPJ cortex, an area implicated both in regulating the VOR and in detecting the unexpected or novel stimuli: thus only vestibular stimulations with these characteristics would produce modified responses.

Cerebellar disorders might also be a contributory element in the observed results as cerebellar lesions can induce increased vestibular responses (Leigh and Zee, 1999). Wu *et al.* (1991) showed that 32 h of sleep deprivation reduced cerebellum glucose metabolism. However, when there is a cerebellar lesion, the VOR time constant is also reduced (Thurston *et al.*, 1987), whereas in our study it remained unchanged. This makes cerebellar disorders an unlikely explanation for our results.

In the earlier studies, no significant modification of the VOR was detected before 24 h of deprivation, and the VOR gain decreased only after 2 days of deprivation (Collins, 1988). It may therefore be supposed that sleep deprivation gradually reduces the VOR gain but that this effect only becomes significant in cases of long-duration deprivation. For impulsive stimulations, this gain decrease may be masked by an

activation of the system for redirecting attention when sleep deprivation remains of short duration. In Collins' study, the subjects were military personnel, a population liable to go without sleep for long periods, which is not the case with the population at large. The duration used in our study, 26–29 h, is one more commonly experienced by the general public (students, shift-workers, jet-lag). It is therefore interesting to note that even this short-duration sleep deprivation can have effects on the vestibular function and hence possibly on the subject's perception of body motion in space. It would therefore appear necessary to assess its impact in real-life operational situations involving the subject's orientation in relation to his/her surroundings, e.g. when driving a vehicle.

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