Motion sickness occurrence does not correlate with nystagmus characteristics

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Abstract

The purpose of this study was to test the hypothesis whereby eye movements as such may be an important factor in the development of motion sickness (MS). The horizontal eye movements of 27 subjects were measured during earth vertical axis rotation (EVAR) and during off vertical axis rotation (OVAR). Two groups were set up, one including subjects who suffered severe MS during the test, and the other including subjects with no MS symptoms. We found no differences in nystagmus parameters (EVAR: gain and time constant; OVAR: eye velocity modulation and eye position modulation) between the MS and the non-MS groups. We can conclude that eye movements are not involved in the development of MS.

Keywords: Motion sickness; Off vertical axis rotation; Eye movements; Vestibular; Vestibulo-ocular reflex; Nystagmus

The mechanism whereby sensory stimulation leads to motion sickness (MS) has not been established. There do exist, however, a number of theories to explain under what conditions MS may occur. Almost all these theories postulate that MS occurs when there is a mismatch between sensory signals (visual, vestibular, and somesthetic) and prediction of such inputs made by the central nervous system. For instance, in the so-called sensory rearrangement theory [10], this prediction comes from the neural store, a kind of memory which retains traces of previous combinations of sensory signals. In the coherence model, this prediction is built up indirectly from the other sensory inputs, with no memory being brought into play [1,3].

From the observation that a local retrobulbar anesthesia induces a reduction in the incidence of emesis and nausea after strabismus surgery [7], Ebenholtz et al. [4] recently put forward an alternative hypothesis: sensory stimulations cause MS not directly but through the eye movements that they induce. Eye movements increase the level of traction exerted on the extra-ocular muscles and this traction elicits an afferent signal that could directly or indirectly stimulate the vagus nerve. Such a reaction would be an attenuated form of the oculo-cardiac reflex. In what follows, we will call this hypothesis ‘the eye movement hypothesis of MS’.

If the traction exerted on the extra-ocular muscles is what constitutes the important information in triggering and establishing MS, we must expect to find a correlation between the nystagmus characteristics and the symptoms of MS. The eye movement hypothesis of MS received some empirical support from Hu et al. [8]. These authors found that during optokinetic stimulation the severity of MS relates to the frequency of eye nystagmus. However, in this study, changes in the frequency of eye nystagmus were induced by changing the spatial frequency of the stripes of the rotating drum. With regard to sensory conflict, a change of stimulation parameters is enough to account for a change in occurrence of MS. Thus, varying the spatial frequency of the stripes on the rotating drum can modify both the frequency of nystagmus and the intensity of MS by independent pathways. Arising from the same cause, i.e. variation of the visual stimulation, these two variables can be correlated although there is no causal relation between the two. One way of overcoming this ambiguity is to keep the stimulation constant and compare the nystagmic response of subjects in whom stimulation caused sickness with that of subjects who were not sick. The aim of this study was to test the eye movement hypothesis of MS using a vestibular stimulation made up of an off vertical axis rotation test (OVAR), a per-rotatory test and a post-rotatory test. The OVAR test is ideal for our purpose as it has been established that well-defined compensatory eye movements can be evoked by this stimulation and that it is highly effective in evoking MS.

A population of 27 subjects, aged from 18 to 41 years...
(23 ± 4.9 years) including 16 males and 11 females was studied. Each subject received a medical examination so as to exclude any individuals with a neurological, vestibular or visual pathology or currently receiving drug therapy.

The vestibulo-ocular reflex was evaluated using a rotatory chair that can be tilted with respect to gravity. The subjects were seated on the rotatory chair with their heads upright. All testing was performed with the subject’s eye open in darkness. The paradigm was composed of two identical sequences, except the direction of rotation, which was inverted from one sequence to the next. For each direction of rotation, the test involved three stages: (i) an earth vertical axis rotation (EVAR). The chair rotation velocity rose from 0 to 60°/s in 0.6 s. The consequence of this is to stimulate the horizontal canal receptors, which are sensitive to angular accelerations. When the head is rotated at constant speed, we observe a compensatory per-rotatory nystagmus whose slow phase velocity decreases following an exponential curve (per-rotatory stimulation). (ii) An OVAR. After 120 s of rotation, the effects of semicircular canals stimulation by the initial angular acceleration had completely vanished. The rotation axis was then tilted to 15° in 2.5 s and kept tilted for 120 s, while a constant rotation velocity was maintained. OVAR induces a cyclical ocular response of otolithic origin of the same frequency as the movement of the chair (see Fig. 1). Recording of OVAR-induced nystagmus started 60 s after tilting, when the bias was established, and lasted for 60 s. (iii) A second EVAR. After 120 s of OVAR, the axis was repositioned vertically and rotation continued at constant velocity for 60 s, the time required for the effect of OVAR to wear off. Then the rotation was suddenly stopped in 0.6 s causing an additional stimulation of the semi-circular canals, but this time in the other direction. On the basis of a previous study performed in the laboratory [3], the stimulation parameters (60°/s, 15° tilt) were chosen to make the examination moderately nauseogenic.

Horizontal eye movements were recorded by an infrared light reflection eye-tracking system (Iris, Skalar, Delft, The Netherlands), then sampled on-line at 100 Hz. Eye movement 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.

During EVAR, slow phase velocity (SPV) curve of horizontal nystagmus was modelled according to the formula

$$\text{SPV}(t) = B + A \cos(2\pi t/T + \phi)$$

where $t$ is the time and $T$ the period of rotation. Magnitudes $B$, $A$ and $\phi$ are, respectively, the bias, the amplitude of modulation and the phase. The only variable used in this study was the amplitude of horizontal modulation. This same analysis was also applied on the eye position, which is a better measurement of the stretching of the extraocular muscles. The mean value of the horizontal modulation was then calculated from the values obtained during clockwise and counterclockwise examinations.

After the first and after the second sequence of rotation, the subject was asked about his (her) sensations and a MS intensity score was established using Graybiel’s table [5]. Out of the 27 subjects studied, nine were not ill (score = 0), ten felt a slight or a moderate malaise (score < 8), and eight suffered a severe malaise or frank sickness (score > 8). Subjects with slight or moderate malaise were discarded and two groups were set up, one including subjects which suffered severe MS during the test (vomiting, retching or marked nausea; mean MS intensity score = 10.5), the other including subjects with no MS symptoms.

Table 1 presents the ocular response parameters of the non sick and sick subjects. OVAR induced eye movements of mean peak-to-peak amplitude of approximately 12°. As the vestibular test used in this study elicits large eye movements and is moderately nauseogenic, it is relevant to the study of the eye movement hypothesis of MS. However, during this vestibular test, individuals displaying symptoms of MS showed eye movements that were no different from those of individuals who were not motion sick (Student $t$-test). These results are therefore in conflict with the eye movement hypothesis of MS.

Guedry [6] showed that very nauseogenic stimulations, such as Coriolis stimulation, could produce smaller ocular responses than less nauseogenic stimulations (EVAR). These results suggest that, to induce MS, eye movements are less important than the stimulation characteristics. However, they do not rule out eye movements as being involved as a secondary factor. By comparing responses of sick and non-sick subjects during the same stimulation, our results permit us to go further and state that the characteristics of eye movements are a negligible factor in the triggering and establishment of MS, at least with vestibular stimulation.

However, in this study we recorded horizontal eye movements only. It would be interesting to repeat this experiment using the same stimulation but recording eye movements in...
Fig. 1. Horizontal eye movement recordings during OVAR for one subject. Positive values indicate a rotation of the eyes toward the right and negative values, a rotation toward the left. During OVAR, there is a cyclical ocular movement (b,c) having the same frequency as the rotating chair (a). Modulation of horizontal eye position and modulation of slow phase velocity are calculated respectively from curves (d) and (e), which represent eye position (d) or slow phase velocity (e) in function of the rotary chair position (in °). (d,e) Superimpose the ten cycles.
three dimensions (by adding torsion and vertical eye movements).

In an earlier study we showed that overall susceptibility to MS was negatively correlated to horizontal modulation amplitude during OVAR and positively correlated to the per/post rotatory time constant [9]. In the present study, we used the same experimental protocol without highlighting any correlation between vestibulo-ocular parameters and MS symptoms directly produced by stimulation. These two results show that the characteristics of the vestibulo-ocular system determine an overall predisposition to MS but no predisposition specifically to any one type of stimulation. Such an overall predisposition of the vestibulo-ocular system appears to be directly related to the efficiency of the velocity storage mechanism [9].

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**Table 1**

Mean values ± SD of nystagmus parameters for non-motion sick (first column) and motion-sick subjects (second column)*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Non-MS subjects (n = 9)</th>
<th>MS subjects (n = 8)</th>
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<tbody>
<tr>
<td>MS score = 0</td>
<td>12.88 ± 2.82</td>
<td>13.25 ± 1.83</td>
</tr>
<tr>
<td>Gain</td>
<td>0.76 ± 0.18</td>
<td>0.77 ± 0.24</td>
</tr>
<tr>
<td>Slow phase velocity modulation (°/s)</td>
<td>6.40 ± 2.66</td>
<td>6.25 ± 2.98</td>
</tr>
<tr>
<td>Eye position modulation (°)</td>
<td>6.53 ± 2.33</td>
<td>5.97 ± 2.93</td>
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</tbody>
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*Results of the comparisons between the two groups (results of Student t-tests) are shown in the final column.