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THREE DIMENSIONAL EYE MOVEMENT ANALYSIS DURING OFF VERTICAL AXIS ROTATION IN HUMAN SUBJECTS

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INTRODUCTION

The earth vertical rotation (EVAR) is one of the most common methods of stimulation for evaluating the function of the semicircular canals. On the other hand, rotation about the axis tilted from the earth vertical (OVAR), which was described and discovered almost simultaneously by Guedry (13) and Benson (2) has been used to investigate the response to combined semicircular canal and otolith organs. Such stimulation induces nystagmus with the mean eye velocity in the direction opposite to the direction of head rotation called as "bias component (BIC)" and the sinusoidal modulation around the mean called as "modulation component (MOC)". These characteristics of the eye movements induced by OVAR are observed in rats (18), cats (9, 16), monkeys (1, 4), and also in human subjects (2, 8, 10, 14).

The BIC and MOC were clearly observed in the horizontal eye movement during OVAR in human subjects (10, 12). On the other hand, the presence of BIC in the vertical eye movement is still controversial in humans (10, 11, 17). In addition, there is no report regarding the torsional eye movement during OVAR in human subjects. The methods for recording and analyzing the eye movements were mainly done using electro-oculography (EOG) (2, 10, 14). EOG can, however, permit only a two dimensional analysis of eye movements, the horizontal and vertical. Thus the torsional eye movement, which is thought to be an essential movement in relation to the otolith-ocular reflex, has not been fully understood yet, especially in humans. In this study, we performed a three dimensional analysis of eye movements during OVAR was performed to investigate the dynamic otolith function in normal human subjects using a computerized image recognition technique developed by us (24-26).

METHODS

Thirty-seven healthy human subjects (thirty men and seven women; ages 21-36 with means of 25.2 ± 3.1 years) participated in this study. The subjects had no known history of oculomotor or vestibular abnormalities. All subjects gave informed consent to participate in this study. The subjects were rotated in a computer-controlled chair in a spherical dome which can be tilted by hydraulic pressure up to 40 degrees from the earth vertical position. The head was positioned at the center of the axis of rotation and was fixed in a comfortable up-right position. The subject was secured by a body harness and soft rubber.

Clockwise rotation at a velocity of 4 deg/sec^2 was applied until the rotation speed reached upto 60 deg/sec after which a constant velocity was maintained. Thus, one full rotation took 6 seconds. After cessation of the per-rotatory nystagmus as monitored on a TV screen, the spherical dome with the rotation chair was tilted to 30 degrees at a velocity of 1 deg/sec and this position was maintained for 60 seconds. During this period the eye movement was recorded on a video tape recorder and analyzed off-line. After the 60 seconds tilt, the subject was returned to an up-right position at a velocity of 1 deg/sec, and a deceleration of 4 deg/sec^2 acceleration was applied until the rotation was terminated.

The eye movement was recorded from the subject's left eye in complete darkness by an infrared CCD camera mounted on the specially designed light weight goggles. Four light-emitting diodes were fixed on the inner surface of the spherical dome along the horizontal and vertical planes separated by 10 degrees for determining the coordinates of the eye position using the right eye. The right eye was then covered during the experimental sequences. To analyze the eye movements three dimensionally, we used the updated version of our standard computerized image recognition method which has been reported elsewhere (25). In brief, the output video signals from a video tape recorder were fed into the hard disk of the computer through an AD converter. A gray-level histogram was created from the digitized image and thresholding was selected to produce binary image at the gray level of the pupil. From this binary image, the center of gravity of the pupil could be calculated, which was then used for analyzing the horizontal and vertical eye movements. To calculate the torsional eye movement, the edge detection filter was applied and 5 to 7 iris striations which had clearly detected the edge were chosen using a computer. By monitoring each of the positions of these clear edges in relation to the center of the pupil, it was possible to calculate the angles of the torsional eye movements.

In seven subjects, the relationship between the eye position and the head position was measured. In these subjects, both the eye and the chair positions were recorded on videotape. The eye position data was fitted with least square sinusoids. From this, the mean horizontal, vertical, and torsional eye position and phase with respect to the chair position were determined. The left ear down (LED) position was taken as the origin of the phase plots. The maximum eye position to the right, upward, and clockwise, with respect to LED was used to the phase lag from the origin (zero).

Statistical analysis was performed using ANOVA test.

RESULTS

Figure 1 gives an example of a 3D analysis data of eye movements in relation to the head orientation during OVAR. During the acceleration period (clockwise rotation), mainly the horizontal nystagmus towards the right was observed. This nystagmus gradually disappeared with time during the constant velocity period. However, when the orientation of the gravity was changed by tilting the spherical dome to 30 degrees, we observed eye movements with all three components (Fig. 1A). These eye movements continued as long as the OVAR was maintained. The horizontal, vertical and torsional eye movements exhibited regular periodic amplitude changes (MOC) in its eye position as shown in Figure 1A, Figure 1B shows the traces of the eye position after removing the saccades using a computer program. As shown in the figure, the eyes deviated at a velocity of 1.3 deg/sec towards the left which has been called as BIC with the MOC mentioned above. On the other hand, no such clear eye deviation was observed in the vertical and torsional eye movements.

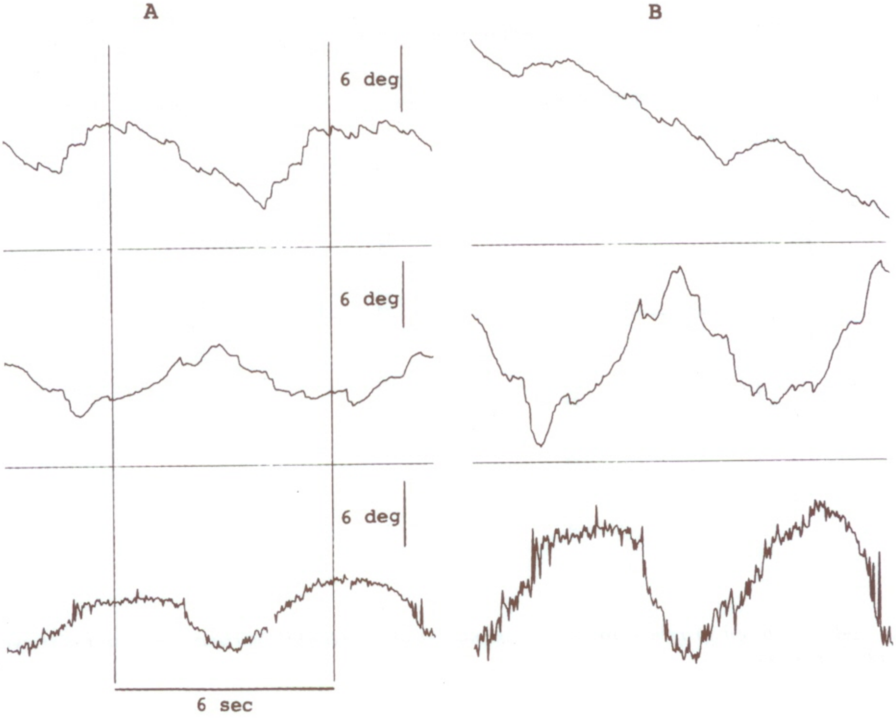

Fig. 1. - *An example of a 3D analysis of eye movements during OVAR (A) and the traces of these eye movements after removing the saccade (B).*

The vertical lines indicate the left ear down (LED) head position. The traces from top to bottom show the horizontal, vertical and torsional eye movements. The upward deflection of these three traces indicates to the right, up and clockwise (from subjects view), respectively (same in Fig. 4).

Figure 2 shows the scattered graph of the BIC of the horizontal, vertical, and torsional eye movements, in each subject. The BIC was measured after removing the saccadic eye movements. The mean and standard deviation of the BIC in the horizontal, vertical, and torsional eye movements in all subjects tested were -2.45 ± 1.36 deg/sec, 0.05 ± 0.89 deg/sec, and -0.06 ± 0.28 deg/sec, respectively. The BIC in the horizontal movement which was directed towards the left, was clearly bigger than that in the vertical ($p < 0.0001$) and torsional ($p < 0.0001$) movements. However, no statistically significant difference was found between the vertical and torsional eye movements ($p = 0.6261$). The direction of the BIC in the vertical and torsional components showed no clear tendency deviating towards one direction, such as upward or clockwise.

The amplitudes (MOC) of the horizontal, vertical, and torsional eye movements were measured in each subject and demonstrated in Figure 3. The mean maximum amplitude and standard deviation of horizontal, vertical, and torsional eye movements were 3.93 ± 1.55 deg, 2.7 ± 0.98 deg, and 4.47 ± 1.8 deg, respectively. The

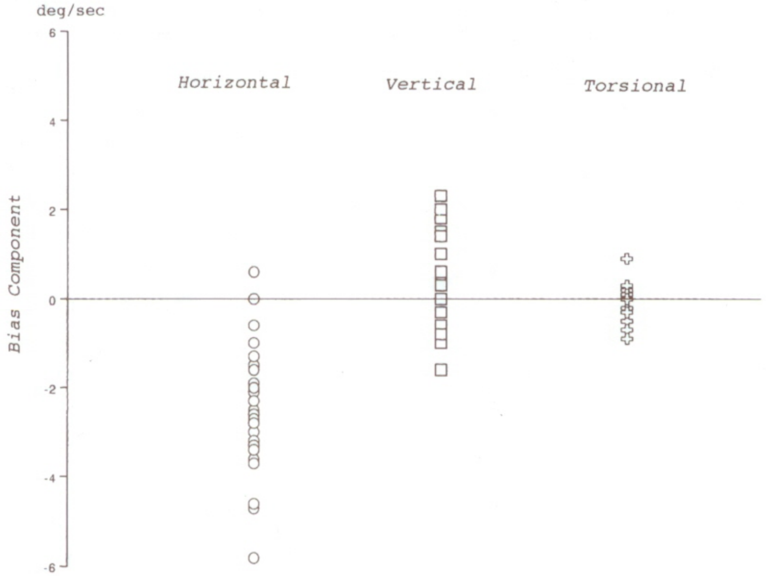

Fig. 2. - *The scattered graph of the bias component of horizontal, vertical and torsional eye movements in each subject.*

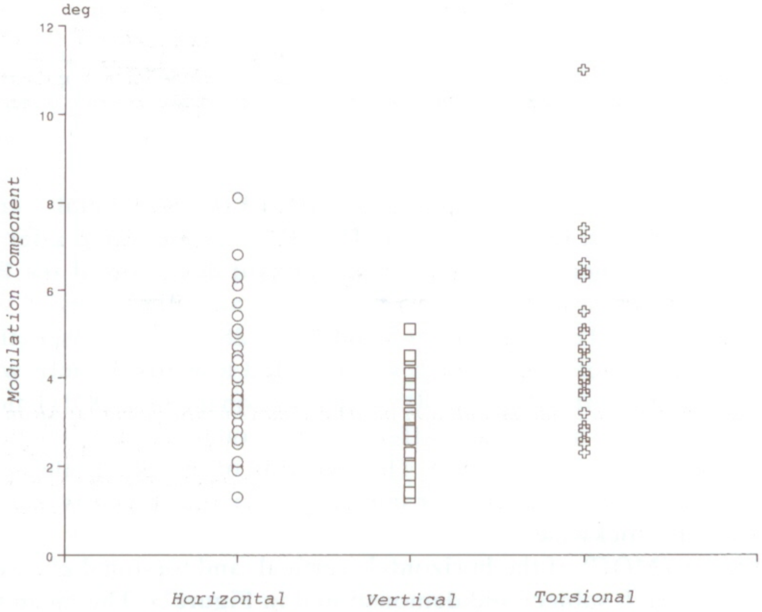

Fig. 3. - *The scattered graph of the modulation component of horizontal, vertical and torsional eye movements in each subject.*

amplitude of the vertical eye movement was significantly smaller than that of the horizontal ($p = 0.0005$) and torsional ($p < 0.0001$) eye movements. There was nostatistical significant difference between the amplitude of the horizontal and torsional eye movements ($p = 0.1218$).

The peak of the MOC of 3D eye movements had different phases. The phase of the MOC in relation to the head position was measured in 7 subjects as mentioned in the material and methods. Figure 4 shows an example of horizontal (right), vertical (upward), and torsional (clockwise) eye movements in relation to the LED position of fitting with least square sinusoids. The average and standard deviation of the phase lag of horizontal, vertical, and torsional eye movements with respect to the origin were 270.6 ± 48.5, 284.4 ± 73.9, 11.6 ± 22.2 deg, respectively. The phase of the torsional eye movement was very consistent with a small variation between each subject. The phase of the vertical eye movement was less consistent compared to that of the horizontal and torsional eye movements.

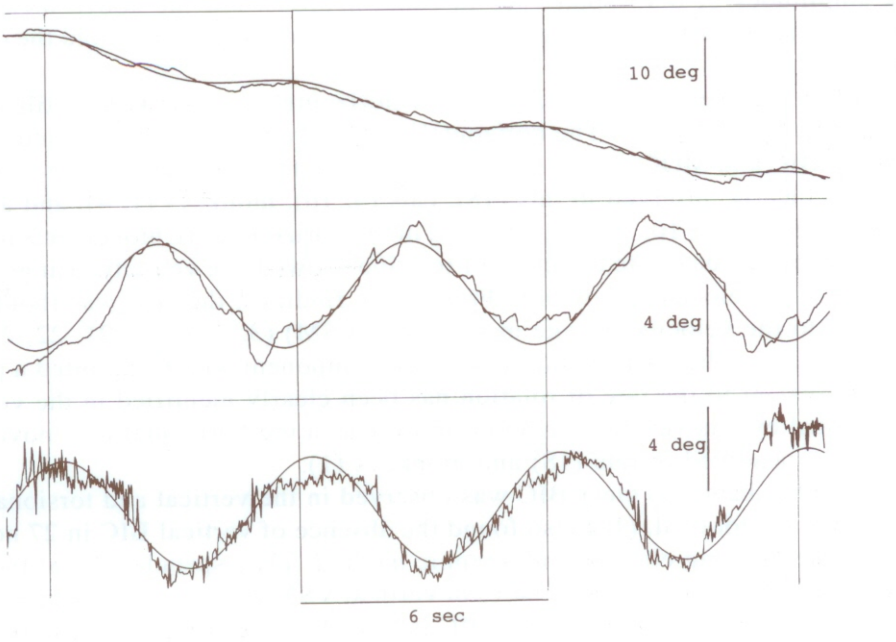

Fig. 4. - *The phase of the amplitude modulation of 3D eye movements during OVAR in one subject.* The fitted sine waves were calculated by the least square method.

DISCUSSION

Off vertical axis rotation using gravity as a linear acceleration by tilting the rotation axis is thought to stimulate the otolith organ. In contrast to the disappearance of per-rotatory nystagmus induced by EVAR, Raphan et al. (22) demonstrated that the per-rotatory nystagmus induced by OVAR in monkeys continued as long as the rotation was maintained. This result is similar to that of EHAR reported by Guedry (14) and Benson (2). They concluded that this nystagmus induce by OVAR was elicited from the otolith organ responding to changes of the direction of gravity to the rotation axis, since the rotational stimuli activates the semicircular canals continuously during EVAR and also during OVAR. In rabbits, Janeke et al. (19) reported that the persistent nystagmus produced by EHA yaw rotation was abolished by bilateral sectioning of the utricular nerves combined with bilateral saccular destruction. Correia et al. (7) inactivated all six semicircular canals by a plugging technique and observed reduction of EHAR induced nystagmus. Cohen et al. (4) found no nystagmus during EHAR in monkeys whose lateral canal was plugged, but clear nystagmus during OVAR. In addition, Goldberg et al. (13) recorded unitary activities of the vestibular primary afferents which innervate the three canals, as well as the otolith organs. They found larger sinusoidal unitary responses with peak amplitudes of 25-75 spikes/sec from the otolith neurons, but weak amplitudes of 0-15 spikes/sec in canal neurons. All the above mentioned data, thus indicate that the nystagmus elicited by OVAR originates from the otolith organs.

OVAR in darkness induced continuous horizontal nystagmus at a tilt of the rotation axis by 30 degrees. The horizontal slow eye velocity had two components, that is the BIC and MOC. These two components in the horizontal eye movements have been clearly observed in rats (18), cats (9, 16), monkeys (1, 4), and also in human subjects (2, 8, 10, 12, 14). The BIC in the horizontal eye movements toward the contralateral side of the direction of rotation showed eye velocity changes with changes of the velocity of rotation. From these findings, the BIC was thought to be related to the velocity storage mechanism (VSM) (3, 5, 9, 13, 21, 22, 23). In the present study, the sinusoidally modulated component which exhibited a periodicity equivalent to the rate of rotation has been clearly identified in the vertical and torsional eye movements, in addition to that in the horizontal eye movement as has been observed in rats (18) and monkeys (1).

On the other hand, no clear BIC was observed in the vertical and torsional eye movements. Darlot et al. (10) also found the absence of vertical BIC in 27 normal human subjects using electro-oculographic method. They speculated that the reason for this is due to the characteristics of vertical VSM which has a low pass filter. In their experimental conditions, the BIC is thought to be completely filtered out, so that the output of the VSM would be zero, even when the vertical system has VSM. Harris et al. (17) reported that there was a small amount of vertical BIC with upward direction in 7 normal human subjects during EHAR using a search coil technique, although the BIC in each subject tested was quite variable. On the other hand, Denise et al. (11) reported that there was no BIC of the vertical eye movements in 39 normal human subjects as have been observed by Darlot et al. (10). Our experimental results and these reports mentioned above, thus indicate that BIC of the vertical eye movement may be absent, or if it is present, it should be quite weak.

In our experiment, the torsional eye movement also showed no BIC. The reason for this result is not yet known. In this context, Darlot et al. (10) speculation as mentioned above may also explain this result, that is the presence of the low pass filter of the VSM in the vertical eye movements. The origin of vertical eye movement in OVAR may be in the saccule due to their response to the position of the head during OVAR. On the other hand, the torsional eye movement seems to be induced by the utricle based on their behavior during OVAR. The mechanism of the absence of BIC in vertical and torsional components may or may not be the same. It is well known that the VSM is quite different between different animal species as shown in the behavior of OKAN (3, 6, 15). In the monkeys, the gradual increase of the slow phase velocity after the rapid rise of OKN respond to the visual stimuli and strong OKAN after the cessation of visual stimuli which are related to VSM were clearly observed (3). While, in humans, the gradual increase of OKN is not clearly observed and also quite weak OKAN is demonstrated (20). In the rhesus monkey also, clear BIC was observed in the vertical and torsional eye movements in addition to the horizontal BIC during OVAR (1). These findings may explain the reason why little or weak BIC was found in humans compared to that in monkeys.

The phase difference of MOC between horizontal, vertical, and torsional eye movements was observed in this study. The torsional eye movements showed quite consistent modulation of the amplitude in respect to the head position. The maximum clockwise torsional eye deviation was observed in the LED head position with a phase lag of 11.6 deg ± 22.2 deg, as mentioned in the results. On the other hand, the phases of the horizontal and vertical eye movements were inconsistent compared to that of the torsional eye movement. Especially, the phase lag of the vertical eye movement was less reliable, since the modulation of the amplitude of the vertical eye movement was clearly smaller than that of the horizontal and torsional eye movements. In addition, the sinusoidal modulation of the vertical eye movement was quite sluggish in many of the subjects tested.

Darlot et al. (9) speculated that the vector along interaural and rotational axes which lies within the frontal plane, induces maximum ocular counter-rolling and horizontal eye deviation. If this is the case, the phase of the horizontal and torsional eye movements should be the same. However, as mentioned above the average phase lag of these two eye movements differ by about 100 degrees, in this study. Therefore, the theoretical calculation proposed by them is not appropriate. In addition, they exhibited no clear average data and demonstrated only data from two subjects. From these results, in human subjects, there should be some differences in the dynamic functional polarity of the utricular macula between the origin of the torsional and horizontal eye movement, in contrast to that observed in monkeys (1).

SUMMARY

Three dimensional analysis of eye movements during OVAR was performed in 37 healthy human subjects using the computerized image recognition technique

developed by us. The modulation component of eye movement was observed in all three components (horizontal, vertical and torsional), whereas the bias component was only clearly seen in the horizontal eye movement. The phase lag of the torsional component was quite consistent with a small variation between each subject with respect to the head position. The phase of vertical eye movement was, however, less consistent compared to that of the horizontal and torsional eye movements. From these results, in human subjects, there should be some differences in the dynamic function of the otolith system compared to that observed in monkeys.

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