DIFFERENCE IN QUICK PHASES INDUCED BY HORIZONTAL AND VERTICAL VESTIBULAR STIMULATIONS: ROLE OF THE OTOLITHIC INPUT

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Abstract—Quick phases (QPs) induced by horizontal and vertical sinusoidal vestibular stimulations were studied in rabbits, cats, and humans. In all the animals, large and frequent horizontal QPs were observed following yaw stimulation in prone position. By contrast, QPs were almost absent during roll stimulation in rabbits, and they were small and oblique during pitch stimulation in cats and humans. As a result of these differences, the range of gaze displacement induced by vestibular stimulations was greater in the horizontal plane than in the vertical one. We also found that the trajectory of the QPs in rabbits was kept horizontal even when the yaw rotation was off vertical axis of ±45° in the sagittal plane. Moreover, in the rabbit, the rare horizontal QPs induced by roll stimulation did not change their orientation at various pitch angles of roll stimulation axis. The QPs were also analyzed following roll stimulation of the rabbit in supine position. In this condition, in which the otolithic receptors were activated in the opposite way compared to prone position, large vertical QPs were elicited. We concluded that these results provide evidence that the otolithic signal plays a role in controlling occurrence and trajectory orientation of the QPs. © 1997 Elsevier Science Inc.

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Introduction

It has been demonstrated recently that the vestibulo-ocular reflex (VOR) of the rabbit and the cat (1–4) shows remarkable differences in the amplitude and frequency of quick phases (QPs), depending upon the stimulation plane. In fact, yaw stimulations about the earth vertical axis evoke large and frequent horizontal QPs in both animals. Conversely, roll stimulations about the earth horizontal axis do not elicit any vertical QPs in the rabbit, and pitch stimulations about earth horizontal axis elicit only small and oblique QPs in the cat. As a result of the small or null vertical component of the QPs, the eye tends to remain in a compensatory position or close to the orbital center during roll or pitch stimulations. On the contrary, during oscillation about the earth vertical axis, the eye is largely displaced in the horizontal plane far from the midline and in the same direction as the head displacement. Because both animals are characterized by a horizontally elongated retinal visual streak, we suggested that the differences in QP amplitude could be related to the retinal morphology (5–7). If this characteristic is the only reason for the QP differences, we would expect that in humans, who present a well-organized central fovea, almost circular, no difference should exist between vertical and horizontal QPs. To verify this, we repeated the experiments in rabbits and cats and extended these to humans.

Another important question we addressed in this study, concerns the mechanism inducing these QP differences and whether they are a result of differences in the intrinsic properties of the reflexes or depend on the tonic and dynamic
influence of the otolithic receptors. It has been suggested that these differences may be due to the simultaneous activation of the otolithic receptors which occurs only during earth horizontal axis or during off vertical axis oscillation. In our previous articles (2,3), we reported some evidence of such an otolithic control. In the cat, in fact, when the otolithic modulation was increased compared to that of the vertical semicircular canals, a reduction of the QPs amplitude clearly resulted. Furthermore, we the enhancement of the amplitude of the vertical QPs in the cat, when the animal was pitched in the side down position, that is, when dynamic otolithic modulation does not occur.

Therefore, in the present study we analyze, in the rabbit, the effect of the change of the tonic and dynamic otolithic input during vestibular sinusoidal stimulation, by modifying the head and rotation axis with respect to gravity. In addition, we studied the eye response to roll with the rabbit in supine position. In this way, vertical semicircular canals and otolithic receptors were activated 180° out of phase compared to the semicircular canal and otolithic receptor activation in prone position (1). The comparison between the response to roll in prone and supine position could be useful in recognizing a role of the dynamic otolithic stimulation in the control of the vertical QPS.

Materials and Methods

The experiments were performed on 10 rabbits, 5 cats, and 3 humans.

Animals

Surgical preparation. Ten pigmented rabbits and 5 cats were anesthetized with ketamine hydrochloride (50 mg/g), xylazine (6 mg/g), and acepromazine maleate (1.2 mg/g), to fix 4 stainless steel screws to the calvarium aligned in a stereotaxic apparatus so that the lambda suture was 1.5 mm above the bregma suture. A small dental acrylic socket was then secured to the animal's skull so that when the head-restraining device was attached to the socket, the animal's head was fixed in a 12° (rabbits) and a 28° (cats) nose down position from the stereotaxic 0° to align the horizontal semicircular canals in the yaw stimulation plane.

Eye position recording. The eye movements were measured in the dark by infrared light projection technique. Under local anesthesia (oxibuprocome 0.4%), a tiny suction cup bearing a light-emitting diode (LED) was attached to the cornea. The LED projected a narrow beam of infrared light onto a photosensitive X-Y position detector (SC-50, UDT, USA) that was fixed relative to the head. the detector provided continuous X-Y indication of the position of the beam’s incident centroid. It was found to be linear to within 5% for eye displacements of ±15°, with a sensitivity of 0.2 min of arc (1).

Vestibular stimulation. All of the experiments were done in the dark. The animals were placed in a cradle and their heads secured at the rotation center of a triaxial servocontrolled rate table (3M-3000, Mangoni, Italy). Table movements were measured by a servopotentiometer. All the animals were sinusoidally oscillated (0.2 to 0.4 Hz, 20° peak to peak) about their vertical axis (yaw stimulation) to evoke horizontal eye responses—the rabbits about their longitudinal axis (roll stimulation) and the cats about their interaural axis (pitch stimulation) to evoke in both the animals vertical eye responses. The rabbits were also variously statically pitched (0°, ±10°, ±20°, ±30°, ±45°, ±180°) and stimulated about their pitched yaw and roll axes.

Data analysis. Eye position and stimulus signals were stored on a magnetic tape recorder (Store D4, Racal Recorders Ltd., UK) and displayed on a digital storage oscilloscope (TDS 420, Tektronix, USA). Signals were digitized off-line by a 12-bit AD converter board (AT-MIO-16E-2, National Instruments, USA) with a sampling rate of 200 Hz, digitally differentiated to obtain the eye velocity signal. Gain was calculated as the ratio between eye and table peak velocities. Fast phases were then separated from the slow phase by using a specific computer program that recognizes automatically the initial and final point of the QPs. Thereafter, slow and fast responses to half cycle stimulation were summed separately to get the cumulative eye displacement due to slow or to fast eye movements. Gaze
displacement was also obtained by computer, adding the table position to the eye position.

**Humans**

*Subjects.* Data were collected from 3 subjects, aged 30 to 48 years, none of whom had a history of neurologic, otologic, or ophthalmologic disorders. Informed consent was obtained from all subjects before they embarked on the study. Experiments were performed in accord with the standard of the committee on human experimentation of MRC Human Movement and Balance Unit (London).

*Eye position recording.* The horizontal and vertical recordings of the movements of the eye were obtained with computerized video-oculography (VOG, SMI Berlin: 0.1° resolution, linear up to ±30° in the horizontal and vertical planes) at a frame rate of 50 Hz. The VOG cameras were mounted on a scuba-diving mask supported by occipital straps; an adjustable helmet was further secured to the head with a premolded bite board.

*Vestibular stimulation.* The horizontal stimulation was performed by sinusoidally rotating (40° p-p amplitude, 0.2 Hz) the subject in a rotatory chair, in the dark. The vertical stimulation (40° p-p amplitude, 0.2 Hz) was using a motorized flight simulator (SEGA R-360) with adjustable leg, trunk, and head support. Each trial consisted of 3 cycles repeated at intervals of 5 min. The seat was adjusted so that the pitch axis was aligned with the interaural axis. During the stimulation, subjects were instructed to perform mathematical computations.

**Results**

*QPs during Yaw Stimulation about Earth Vertical Axis and Roll Stimulation about Earth Horizontal Axis in the Rabbit*

In the upright position the rabbit was sinusoidally rotated (20° p-p, 0.2 to 0.4 Hz) about the yaw and roll axes (Figure 1). During yaw stimulation, horizontal slow compensatory eye responses (gain = 0.75 ± 0.06) were interrupted by opposite directed QPs. In most cases, a single QP resets the eye toward the orbital center during half a cycle of stimulation. The amplitude of the QPs was in the range of 6° to 10°. Their trajectories were coplanar with the compensatory slow phases (SPs), showing only small and insignificant deviation from the horizontal plane, always less than 5° (Figure 1). During roll stimulation (20° p-p, 0.2 to 0.4 Hz), the eye responses in the vertical plane were represented by compensatory slow phases alone (gain = 0.78 ± 0.05). However, horizontal QPs were seldom present, displacing the eye along the horizontal meridian. In a few cases, following an unpredictable horizontal eye displacement, the horizontal QPs occurred as a sequence of alternating QPs in opposite directions (Figure 1). As a result of the occurrence of only horizontal QPs, the rabbit's eye varied the horizontal position in space, while it remained fixed in the vertical plane during both yaw and roll stimulation.

*QPs during Yaw Stimulation about Earth Vertical Axis and Pitch Stimulation about Earth Horizontal Axis in the Cat*

We tested the VOR in response to yaw and pitch stimulation at 0.2 to 0.4 Hz (20° p-p) in 5 cats (Figure 2). The pitch stimulation in cats was considered equivalent to the roll stimulation in the rabbit, as it induces vertical eye responses in frontally eyed animals. The horizontal eye responses to yaw stimulation were characterized by high gain of the compensatory slow phases (SPs) (0.82 ± 0.04). The SPs were perfectly aligned with the stimulation plane. Large and frequent QPs (2 to 3 for a half cycle) interrupted the SPs, shifting the eye in the same direction as the head movement. The cumulative QP amplitude (23.2° ± 5.1°) was greater than the SP cumulative amplitude (15.8° ± 4.5°), so that, at the end of half a cycle of stimulation, the eye was clearly displaced in the orbit toward an orbital anticompenatory position, in the same direction as the head movement. The QP trajectories were almost horizontal, with only small deviations from this plane (3° to 8°). On the whole, during 5 cycles of stimulation, the hori-
Horizontal deviation of the gaze (cumulative QP amplitude + stimulus amplitude − cumulative SP amplitude) was about 5 to 7 times greater than the vertical displacement (Figure 2). Conversely, in response to pitch stimulation, frequent vertical QPs were evoked, resetting the eye toward the orbital center. The frequency of QPs (2 to 3 for a half cycle) was similar to that induced by yawing the animal, but their amplitudes were smaller. Therefore, the vertical cumulative
amplitude of the QPs was $10.2° \pm 3.5°$, less than that of the horizontal QPs. Since the vertical SPs showed a gain of about $0.85 \pm 0.05$, at the end of half a cycle of stimulation, the eye remained in a compensatory position. Interestingly, the orientation of the QPs was oblique and directed toward both sides. Their inclination was mostly in the range of $30°$ to $50°$, but in some cases, pure horizontal or pure vertical QPs were evoked. Therefore, as a consequence of the different space distribution of the QPs, in 5 cycles of stimulation, the gaze displacement was 2 times greater than the vertical one (Figure 2).

**QPs in Humans**

The QPs were studied in 3 subjects during yaw and pitch stimulation. During sinusoidal yaw stimulation ($40°$ p-p, $0.2$ Hz), compensatory slow phases (SPs) were interrupted by large and frequent QPs (Figure 3). The reflex gain ranged within $0.7$ and $0.85$. As the cumulative amplitude of the QPs clearly exceeded the cumulative slow phase amplitude, the position of the eye at the end of a half cycle of vestibular stimulation was shifted in the anticomparatory direction. The eye movements were mostly oriented in the horizontal plane, although minor shifts ($5°$ to $7°$) were observed. Because of the horizontal QPs, the eye was largely displaced in space along the horizontal meridian.

During pitch stimulation ($40°$ p-p, $0.2$ Hz), the compensatory SPs were frequently interrupted by oblique QPs (Figure 3). The reflex gain was within $0.7$ and $0.8$. The cumulative amplitude of the oblique QPs was half of that induced by yaw stimulation, while the slow phase amplitude was similar. Because of the reduced amplitude and oblique orientation of QPs, the eye displacement in the vertical plane during pitch stimulation was less than the horizontal displacement during yaw stimulation.

The differences in the QPs were also clearly

Figure 2. Eye responses to yaw (left side) and pitch (right side) stimulations in the cat. Eye position (upper traces) and gaze (lower traces) x-y recordings in 5 cycles of stimulation (cat: $20°$ p-p, $0.2$ Hz). Quick phases are represented by rare dots, and compensatory slow phases are represented by frequent dots. Note that the QPs are large and horizontally oriented during yaw stimulation, whereas they were small and oblique during pitch stimulation.
Figure 3. Eye responses to yaw (left side) and pitch (right side) stimulations in the human. Eye position x-y recordings in 3 cycles of stimulation (40° p-p, 0.2 Hz). Quick phases (QP) are represented by rare dots and compensatory slow phases (SP) by frequent dots. Note the large and horizontally oriented QPs during yaw and the small and oblique QPs during pitch.

QPs during Yaw and Roll Stimulation at Different Pitch Angles of Head-Rotation Axis in the Rabbits

In the upright position, the high frequency yaw stimulation induced both compensatory slow phases (SPs) and quick phases (QPs) lying in the plane of the stimulus, that is, in the earth horizontal plane (Figure 1). However, when the animal was yowed at different head pitch angles, only the SPs remained aligned with the plane of the stimulus, whereas the QPs remained oriented along the earth horizon (Figures 4 and 5). Thus, by increasing the head pitch angle, the trajectories of SPs and QPs increasingly diverged. The frequency and the amplitude of QPs did not change at different head inclinations. The reorientation gain (eye trajectory orientation angle re-orbit/table orientation re-horizon) was close to 1 from 0° to 45° of pitch angle. By rolling the rabbit in the upright position, no vertical compensatory slow responses were induced, but only rare horizontal QPs. However, when the roll stimulation was delivered around a pitched longitudinal axis, horizontal QPs occurred with a frequency that increased by increasing the axis inclination. The trajectory of the QPs was almost horizontal, showing a reorientation gain close to 1. Their frequency was always less than that observed during yaw stimulation (from 0.2 to 0.7 QP for a half cycle). The amplitude showed a 10% to 30% reduction (Figure 4).

Vertical QPs in Response to Roll Stimulation with the Rabbit in the Supine Position (180°)

By rolling the animal in the supine position, VOR resulted from the activation of both vertical semicircular canals and otolithic receptors, but the maculae were stimulated by gravity in the opposite direction compared to the prone position (Figure 6). In the supine position, in fact, the same head oscillation that activates vertical canals as in the prone position causes gravity to act oppositely on the otolithic maculae. In this position, the eye responses showed compensatory slow phases in a direction opposite to that of the stimulus, substantially similar to those obtained in prone position, with only a slight reduction of the gain (at 0.4 Hz gain = 0.56 ± 0.08). However, the slow phases were interrupted by QPs showing the same direction...
Figure 4. Eye responses to yaw and roll stimulations in the rabbit at different head-rotation axis pitch angles. Quick phases (QPs) and compensatory slow phases (SPs) in response to yaw and pitch (0.4 Hz, 20° p-p). Dashed lines indicate the stimulation plane. Note that the SPs are aligned with the stimulus, whereas the QPs remain horizontal.
Figure 5. SPs and QPs orientation relative to the horizon at different head-rotation axis pitch angles in 3 rabbits during yaw (left) and roll (right) stimulations (0.4 Hz, 20° p-p). Abscissa: pitch angle of head and rotation axes (0° = horizon; positive values = nose up; negative values = nose down). Ordinates: Inclination of QPs and SPs relative to the horizon.

of the stimulus. These QPs were large (10° to 15°) and mostly vertical in orientation. They took place at each half cycle and displaced the eye in the orbit in the same direction as the head movement (Figure 6).

Discussion

Our findings confirm that there are differences in the vestibular-induced QPs, depending upon the stimulation plane (1–4). In prone position, vertical resetting eye movements were absent in rabbits, in response to roll stimulation, and they were small in cats and humans, in response to pitch. By contrast, QPs induced by yaw stimulation were always large and frequent. Because of the similarity in the gain of slow phase responses, the horizontal preponderance of the gaze displacement during head movements was provoked only by QP difference in vertical and horizontal plane. Interestingly, in frontally eyed animals, the orientation of these QPs was rarely vertical, and in most cases the QPs had a remarkable horizontal component. We believe that this horizontal preponderance is maintained even when the head moves on the fixed body, as occurs in most natural conditions, since the cervical input is not sufficient to abolish QPs in rabbits (8,9) and does not evoke a consistent effect in frontally eyed animals (personal observation).

It has been suggested (10) that this diversity in QPs could be related to the peculiar distribution of the ganglion cells in the retina and to the visual world continuity during head displacement. Cats and rabbits present, in fact, a horizontally elongated visual streak instead of a central fovea with a narrow vertical dimension of the high receptor density area. Because of that, visual space discontinuity during head displacement could
be induced by large QPs in the vertical plane, but not in the horizontal one. However, humans have a well-defined central fovea, yet we observed similar QP differences. This leads us to take into consideration another aspect, such as the difference in the gaze field amplitude and event frequency. In humans, in fact, the amplitude of the gaze field along the horizontal meridian is greater than that along the vertical one, and the events that mostly elicit animal attention are more likely to occur about the horizontal meridian. These should require an enhancement of the visual scan in the horizontal plane. Therefore, it is possible that the increase in the horizontal gaze displacement during the vestibulo-ocular reflex could be useful for this purpose.

Another explanation for the reduced vertical gaze displacements during vestibulo-ocular reflex could be related to the need to keep constant on the retina the visual reference of the horizon, for a better control of head balance and movements in the sagittal and frontal plane. However, the efficacy of this control appears to be very powerful only in laterally eyed animals. In fact, unlike the rabbit showing a complete absence of vertical QPs, cats and humans present small vertical QPs which reduce the horizon stability on the retina.

Another finding of this paper, obtained from the study on rabbits, concern the gravity influence on the QPs. In fact, the orientation of QPs tends to remain constant in space when varying the position in space of the head and stimulation axes. Furthermore, QPs induced by roll stimulation showed similar gravity influence. They were horizontal although rare in the upright position and remained horizontal when the head and stimulus were pitched. The gravity influence on the orientation of other vestibular and optokinetic responses has already been shown (11–14). A shift of the eye rotation axis after off-vertical axis rotation and after head tilt for both optokinetic afternystagmus (OKAN I) and post-rotatory nystagmus (PRN) has been demonstrated. In addition, the negative optokinetic afternystagmus (OKAN II) has also been shown to be reoriented according to the gravity vector in the rab-
bit (15). However, the reorientation of the PRN and of the OKAN required the charge of the velocity storage. On the contrary, the reorientation of QPs during VOR occurred even during short-lasting vestibular stimulation, which did not induce any spatial re-alignment of the slow phase toward gravity. This suggests that the reorientation of QPs of sinusoidal VOR could be under a different central control finalized to a different eye motor strategy compared to the reorientation of other vestibular and optokinetic nystagmic responses.

In an attempt to explain the mechanism inducing QPs diversity during yaw, roll, and pitch stimulations, the experiments performed in rabbits clearly indicate that the tonic and dynamic influences of the otolithic receptors play an important role in affecting the amplitude, frequency, and trajectory of QPs. We cannot exclude that the vertical canal circuitry is, per se, less powerful in eliciting QPs, but the otolithic influence seems to have a stronger role. In fact, to keep the QP trajectory horizontal in a different head position, the otolithic signal should shift the coordinates of the QPs from orbital to inertial ones. However, the role of the otolithic signal is not limited to maintaining QPs orthogonal to the gravity vector. In fact, the otolithic signal also defines where the QPs should reset the eye along the vertical meridian. During roll in supine position, large and vertically oriented QPs occurred in the opposite direction compared to the slow phases. In this particular condition, the eye is guided by the semicircular canals in the compensatory direction, while the dynamic modulation of the otolithic receptors moves the eye in exactly the opposite direction. In fact, the gravity acts in reverse mode in the supine position. This is not the case when the animal is in prone position, where both semicircular canals and otolithic receptors guide the eye in the same direction. Therefore, to explain the presence of QPs in the upside down position and the lack of vertical QPs in the upright position, the opposite otolithic modulation should be considered. We suggest that the otolithic input induces a shift of the reference point in the vertical plane, toward which the eye should reset. When this shift occurs in the same direction as the oculo-compensatory eye response, as in the upright condition, QPs are not elicited. Conversely, when this point is shifted in the opposite direction, large QPs take place to reset the eye toward that point. This vertical displacement leads the QPs horizontally during vestibular stimulation at different head inclinations. This implies that the position signal controlling the end point of the QPs does not undergo the same central processing of the otolith-ocular reflex (OOR). In fact, in the rabbit (4,16), the OOR shows gain close to 0.1 and phase lag greater than 60° at 0.4 Hz. With these transfer characteristics, the otolithic signal would not be able to maintain the QPs horizontally. On the contrary, we suggest that resetting reference point shift is equal and simultaneous to the actual reflex-induced eye movements.

It has been proposed that the signal originating from the semicircular canals may be capable of exercising quantitative control over the QPs and timing and that eye position information may control the QP generation (17-19). Our data suggest that these internal signals, specifying eye positions at which QPs start and end, can be influenced by an external signal carrying the information of the head position in space. This input can modify the trigger level of the QPs and their trajectory for defining eye position in space.

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**REFERENCES**