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UNIVERSIDAD NACIONAL AUTONOMA DE MEXICO

FACULTAD DE MEDICINA

**ESTUDIO BINOCULAR DEL COMPO-
NENTE VERTICAL DE LA RESPUESTA
VESTIBULO-OCULOMOTORA A LOS
MOVIMIENTOS EN EL PLANO FRONTAL**

TESIS

**Que para obtener el grado de
MAESTRA EN CIENCIAS MEDICAS**

presenta

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México, D. F.

1999

270631

**TESIS CON
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Estudio binocular del componente vertical de la respuesta vestibulo-oculomotora a los movimientos en el plano frontal

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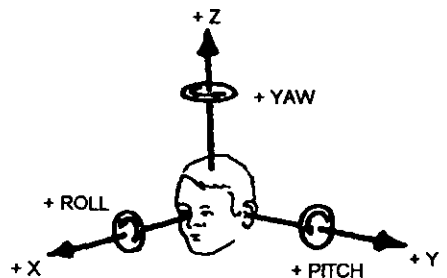
INTRODUCCION

El equilibrio corporal y la orientación en el espacio son producto de la integración de información vestibular, visual y propioceptiva para generar respuestas motoras específicas. El sistema vestibular detecta la posición y movimientos de la cabeza en el espacio. Información que es importante para desencadenar conductas conscientes e inconscientes, como los reflejos para mantener la postura y desviar la mirada. En condiciones naturales, los movimientos de la cabeza en el espacio están constituidos por la combinación de aceleraciones angulares y lineales. En el laberinto del oído interno se encuentran los receptores para la percepción de ambos tipos de aceleraciones. Los canales semicirculares detectan la aceleración angular mientras que los otolitos de las máculas utricular y sacular son receptores de la aceleración lineal y del vector gravitacional.

Cuando se ejecuta cualquier movimiento, es a través de la información laberíntica que el reflejo vestibulo-ocular actúa para mantener estables las imágenes del entorno en la retina (Sharpe 1993). Las características de los músculos extra-oculares permiten que el ojo ejecute movimientos compensatorios en cualquier dirección, principalmente por rotación y con sólo mínima translación (ver Apéndice). Una forma de estudiar la rotación del globo ocular en las tres dimensiones es separando sus componentes en cada uno de los tres planos (Henn 1996):

- axial (yaw) que corresponde a lo 'horizontal',
- sagital (pitch) en relación a lo 'vertical' y
- frontal (roll) para referirse a la 'torsión'.

Con su respectivo eje de rotación (x,y,z), perpendicular a cada plano.



Sistemas de coordenadas

Los movimientos oculares son preponderantemente angulares y por lo tanto no conmutativos. La descripción tridimensional de un mismo movimiento con diferentes sistemas de coordenadas puede conducir a interpretaciones distintas (Carpenter 1988, Howard 1995) (Figura 1).

En el sistema de coordenadas de Helmholtz el eje horizontal, alrededor del cual se efectúan los movimientos verticales, se encuentra fijo al cráneo, mientras que el eje vertical rota en torno al eje horizontal sin mantener un ángulo fijo con respecto al cráneo. En el sistema de Fick es el eje vertical el que se encuentra fijo al cráneo, este sistema es similar al previo cuando se le rota 90°. El sistema de perímetros tiene su fundamento en la presencia de un eje, fijo a la cabeza, que se proyecta desde la órbita hacia adelante y se utiliza para identificar excentricidad de la posición del ojo. Este último sistema esta en relación a la Ley de Listing, en la que se considera que hay un plano fijo a la cabeza que casi coincide con el plano frontal cuando los ojos se encuentran en posición primaria; para cualquier movimiento del ojo se asume que solo hay un eje de rotación (horizontal, vertical u oblicuo), por lo que no se pueden especificar las rotaciones de torsión. Una alternativa para especificar la posición del globo ocular es utilizar vectores de rotación; que en términos de dirección (n) y amplitud ($\tan(\theta/2)$) describen la rotación necesaria para llevar al ojo de una posición de referencia a cualquier otra posición ($r = \tan(\theta/2) * n$) (van Opsal 1993).

La descripción de los movimientos oculares también puede realizarse en términos de la velocidad durante su trayectoria. La velocidad angular (Merfeld 1992) se expresa en coordenadas fijas a la cabeza, con o sin el cálculo de la suma de vectores que identifica los ejes de rotación del ojo en cada plano.

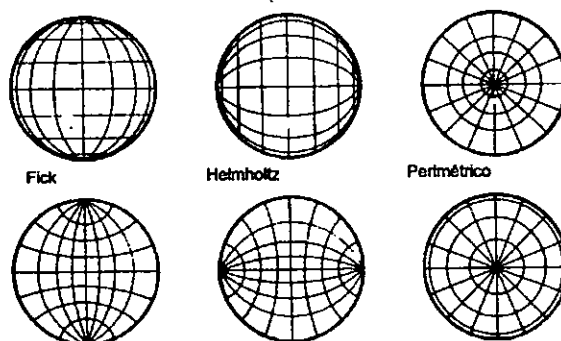


Figura 1. Sistemas de coordenadas que se han utilizado con mayor frecuencia para describir los movimientos oculares.

Métodos de Registro Tridimensional

La electronistagmografía y las técnicas de iluminación infra-roja sólo permiten el estudio de los movimientos oculares en una o dos dimensiones. Por este motivo, el estudio tridimensional de la respuesta vestibulo-oculomotora dinámica estuvo limitado a los planos horizontal y vertical, hasta la introducción reciente de la video-oculografía y la modificación (Collewijn 1985) de la técnica de localización magnética de señales (Robinson 1963).

La video-oculografía utiliza técnicas de procesamiento de las imágenes secuenciales (cuadros) de la video-grabación monocromática del ojo. Mediante el uso de iluminación infra-roja, que es reflejada por el iris y la esclera pero no por la pupila (técnica de "pupila negra"), se rastrea la posición de la pupila (Figura 2). El análisis de las líneas horizontales de los dos campos que componen cada cuadro permite identificar la posición de la pupila horizontal y verticalmente; para determinar la torsión ocular se calcula la posición de marcas radiales del iris seleccionadas para el sujeto en cada cuadro del video (Clarke 1991).

La técnica de registro magnético utiliza la detección de cambios de la amplitud o fase de un potencial de corriente alterna inducido por bobinas ('coils') sensoras conectadas a amplificadores y alineadas con el plano frontal de un campo magnético homogéneo, creado horizontal y transversalmente por un arreglo de 'coils' de registro (Figura 3). La orientación horizontal y vertical del sensor se obtiene directamente de la señal de los amplificadores, cuando se cuenta con una fase de referencia adecuada. La detección de la torsión se efectúa mediante un 'coil' sensor horizontal, perpendicular a la orientación del campo magnético (Collewijn 1985).

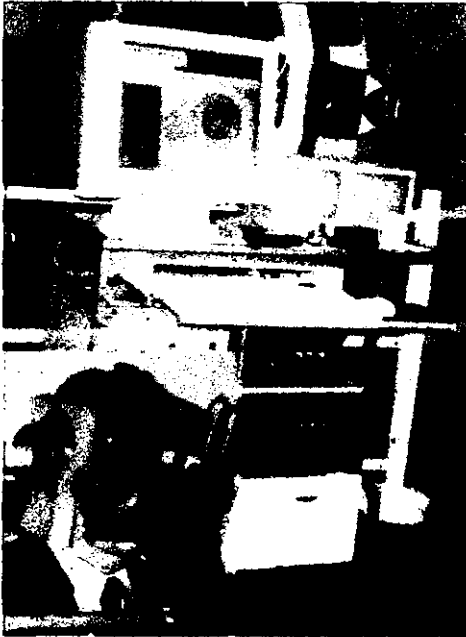


Figura 2. Equipo para registro y análisis de video-oculografía.



Figura 3. Sujeto al centro de un marco donde se genera un campo magnético.

Respuesta vestibulo-oculomotora a los movimientos en el plano frontal

Mediante las técnicas descritas ha sido posible estudiar la respuesta vestibulo-ocular evocada por movimientos cefálicos en el plano frontal, que en este estudio llamaremos rol, la cual tiene un componente estático y uno dinámico. El componente estático es debido a la re-orientación de los otolitos en relación al vector de la gravedad (Diamond 1983) y el componente dinámico a la activación de los canales semicirculares por la aceleración angular (Collewijn 1985).

Las rotaciones de la cabeza en rol producen diferentes respuestas vestibulo-oculomotoras en animales con diferente posición anatómica de los ojos, relacionados a las características cinemáticas de los músculos extra-oculares (Simpson 1981) (Figura 4). Los animales que tienen los ojos en posición lateral, durante movimientos de la cabeza en rol, presentan una divergencia vertical de los ojos acompañada de un componente de torsión pequeño (Tegetmeyer 1982). El mismo movimiento en el ser humano, quien tiene los ojos en posición frontal, evoca principalmente torsión ocular (Collewijn 1985) acompañada de un pequeño componente vertical divergente, recientemente identificado por métodos perceptuales en condiciones estáticas - por estímulo de los otolitos - (Betts 1995) y mediante registro oculomotor en condiciones dinámicas - por estímulo de los canales semicirculares - (Jáuregui-Renaud 1996).

Antes de efectuarse estudios tridimensionales y binoculares, la divergencia ocular vertical asociada a torsión en seres humanos sólo se había identificado en pacientes con alteraciones neuro-otológicas, atribuyéndose a la lesión de la vía otolítica (Wolfe 1993, Halmagyi 1994). Sin embargo, registros video-oculográficos recientes han mostrado que el estímulo de los canales semicirculares verticales, por sí mismo, puede inducir este tipo de movimientos oculares (Jáuregui-Renaud 1996).

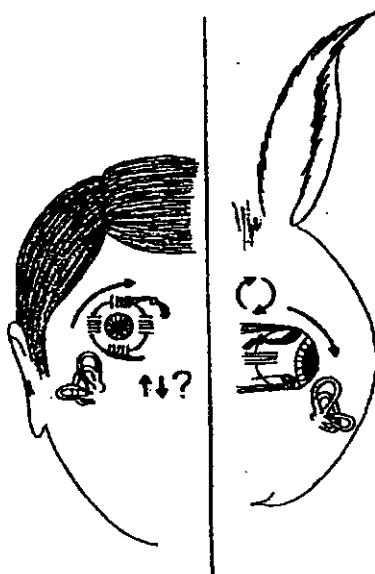


Figura 4. Representación esquemática de los principales componentes de la respuesta vestibulo-oculomotora a los movimientos en rol del ser humano y del conejo

Los conocimientos actuales sobre control oculomotor, son congruentes con que, durante rotaciones de la cabeza en rol, el ser humano efectúe movimientos de torsión conjugados que se acompañen de movimientos verticales disociados. La acción simultánea de los músculos extra-oculares rectos verticales y oblicuos puede producir esta combinación, si la fuerza de contracción de los rectos es mayor que la de los oblicuos (López 1991). El control de los movimientos oculares verticales y de torsión se lleva a cabo por los mismos núcleos premotores del tallo cerebral. El núcleo intersticial de Cajal tiene aferencias excitatorias de los canales semicirculares verticales contra-laterales y aferencias inhibitorias de los canales semicirculares ipsilaterales (Fukusima 1987). En primates, el estímulo unilateral del núcleo

intersticial de Cajal produce movimientos de torsión hacia el mismo lado acompañados de un componente vertical que puede ser hacia arriba o hacia abajo (Crawford 1991).

En animales con los ojos en posición lateral, la divergencia ocular vertical durante los movimientos en rol, permite alinear las estrias visuales de la retina con el horizonte (van der Steen 1984). En el hombre, esta divergencia ocular podría ser vestigial. Sin embargo, debido a que el ser humano tiene localización variable de las foveas hacia el campo temporal de la retina (aproximadamente de 5°), no existe co-linealidad de los ejes visual y óptico (Ditchburn 1987). Hecho que podría ser fundamental para explicar la divergencia ocular vertical durante la torsión. Durante los movimientos en rol, si la línea de la visión coincidiera con el eje de rotación de los ojos, el movimiento compensatorio apropiado sería únicamente de torsión. Sin embargo, cuando se utilizan coordenadas fijas a la cabeza, la localización de la fovea en el campo temporal de la retina podría implicar que pequeños componentes verticales fueran necesarios para conservar la imagen en la fovea (Jáuregui-Renaud 1997) (Figura 5).

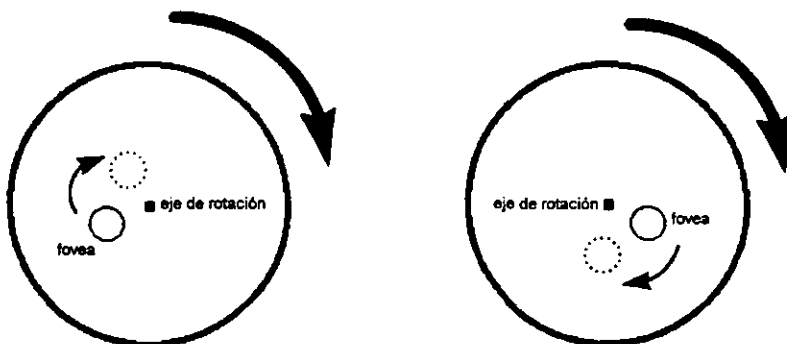


Figura 5. Representación del posible desplazamiento de las foveas durante la ciclorotación conjugada, compensatoria a oscilaciones alrededor de un eje naso-occipital, cuando los movimientos oculares se estudian en un sistema de coordenadas fijas a la cabeza.

El análisis de las respuestas durante la fijación visual y con variaciones en el ángulo de convergencia ocular horizontal contribuye a esclarecer si la divergencia vertical de los ojos asociada a la torsión ocular está en relación a la falta de co-linearidad entre los ejes visual y óptico. Debido a que, durante la respuesta vestibulo-oculomotora, los ejes de rotación de los ojos se encuentran fijos en relación a la cabeza (Crawford 1991b) la modificación del ángulo entre los ejes visuales de ambos ojos podría producir variaciones en la disparidad vertical evocada por la torsión ocular.

Justificación

El presente proyecto se efectuó para investigar las características binoculares de la respuesta vestibulo-oculomotora a los movimientos en rol, con particular atención al componente vertical, y su posible modulación por la fijación visual y por la vergencia ocular horizontal.

En diferentes estudios del proyecto se utilizaron los dos métodos que existen para registrar los movimientos oculares en tres dimensiones. El estímulo rotatorio se planeó para investigar, con especial énfasis, la respuesta oculomotora evocada por los cambios de la información proveniente de los canales semicirculares verticales, con y sin modificación de la aferencia de los otolitos. Los registros se efectuaron durante rotación sinusoidal y después de rotación a velocidad continua, para verificar la posible influencia de factores que durante la rotación pudieran distorsionar las características tanto de la fase lenta (vestibular) como de la fase rápida (de re-fijación visual) de la respuesta oculomotora ; se procuró minimizar la intervención de posibles artefactos que pudieran contribuir a interpretaciones equívocas de los hallazgos.

ETAPA I.

Documento de referencia al final del capítulo, publicado en: *Acta Otolaryngol (Stockh) 1998;118:170-6*

Contribución de los otolitos y de los canales semicirculares a la respuesta binocular humana a la oscilación en rol

Los movimientos en rol producen aceleración angular, que estimula a los canales semicirculares y re-orientación del vector gravitacional con respecto a los otolitos. Además, durante la rotación, la visión del entorno constituye un estímulo optocinético que aumenta la ganancia de los movimientos oculares compensatorios.

Objetivos y Metodología

Para investigar la contribución de los otolitos y de los canales semicirculares y la influencia visual en la respuesta vestibulo-oculomotora del ser humano a los movimientos en rol, tres sujetos jóvenes, de 25 a 30 años (2 mujeres), sin enfermedad neuro-otológica, aceptaron ser sometidos al siguiente protocolo de estudio:

- Oscilación de todo el cuerpo alrededor del eje naso-occipital en posiciones sedente erguida y decúbito supino (Figura 1), a 0.1 Hz ($27 \pm 4^\circ/s$ y $25 \pm 3^\circ/s$) y 0.4 Hz ($68 \pm 8^\circ/s$ y $72 \pm 4^\circ/s$), en la oscuridad.
- Oscilación de todo el cuerpo alrededor del eje naso-occipital en decúbito supino, a 0.1 Hz ($27 \pm 3^\circ/s$) y 0.4 Hz ($76 \pm 5^\circ/s$), con fijación visual en una imagen compleja (un bosque) fija a la tierra.

Para estudiar con más detalle la influencia de los canales semicirculares verticales en las características de la respuesta oculomotora, los mismos sujetos fueron expuestos a:

- Oscilación de todo el cuerpo, en posición sedente erguida, alrededor de ejes 'oblicuos' orientados a 20° y 40° a cada lado del eje naso-occipital (horizontales con respecto a la tierra), a 0.4 Hz ($70 \pm 6^\circ/s$).

Para verificar la influencia de los canales semicirculares horizontales sobre el componente horizontal de la respuesta, uno de los sujetos aceptó participar en un procedimiento complementario:

- Oscilación en la oscuridad a 0.4 Hz ($63 \pm 3^\circ/s$), en decúbito supino con el cuello en flexión o extensión para colocar la línea de Reid de su cabeza a 23° , 6° y -12° con respecto al eje de rotación (vertical con respecto a la tierra), ubicado en el plano sagital medio del sujeto.



Figura 1. Posiciones en las que se oscilo a los sujetos (sedente erguido y decúbito supino).

Los movimientos oculares se registraron con equipo para video-oculografía computada. El estímulo rotatorio, generado manualmente, se registró mediante un potenciómetro. La ganancia se definió como la proporción que resulta de dividir la velocidad durante la fase lenta del nistagmus entre la velocidad del estímulo. El análisis del componente vertical disconjugado se efectuó en el trazo que se obtuvo al sustraer el registro del ojo izquierdo al del ojo derecho.

Resultados y Comentarios

La oscilación de los sujetos, en todas las condiciones, indujo movimientos oculares principalmente de torsión, acompañado de pequeños movimientos horizontales conjugados y movimientos verticales disconjugados. El ojo que mostraba intorsión se movía hacia arriba mientras el ojo con extorsión se movía hacia abajo. La evidencia de disociación vertical de los ojos en ambas posiciones (sedente erguida y decúbito supino) es evidencia de que en el ser humano, sin enfermedad, el estímulo de los canales semicirculares por si mismo puede evocar movimientos oculares verticales disconjugados.

Los registros en la posición sedente erguida, comparada con el decúbito supino, mostraron tendencia al incremento de las ganancias de velocidad. Sin embargo, la diferencia para el componente de torsión fue significativa sólo para un sujeto (a 0.1 Hz y 0.4 Hz) y para el componente vertical disconjugado para dos sujetos (a 0.4 Hz) (ANOVA, $p < 0.05$). Estos resultados indican que, a las frecuencias estudiadas, la contribución de los otolitos para la respuesta de torsión es insignificante.

Durante la oscilación con fijación visual, la ganancia del componente de torsión aumentó en los tres sujetos pero la ganancia del componente vertical disconjugado aumento sólo en dos, aparentemente porque en el tercer sujeto la convergencia horizontal de los ojos en la luz fue

menor que en la obscuridad, al contrario de lo que sucedió en los otros dos sujetos. La presencia de disociación vertical de los ojos con y sin fijación visual es evidencia de que ésta forma parte de la respuesta humana al rol. La asociación entre la magnitud de la convergencia horizontal y la amplitud de la divergencia ocular vertical es un hallazgo que requiere estudios específicos (ver Etapa II).

La oscilación alrededor de ejes de rotación oblicuos provocó movimientos oculares verticales asimétricos, ambos ojos se movían en la misma dirección pero uno se movía más rápido que el otro. Cuando el eje de rotación estuvo a la izquierda del sujeto los movimientos verticales del ojo derecho fueron más amplios y más rápidos que los del ojo izquierdo y *viceversa*. Durante este tipo de oscilación el patrón de activación de los canales semicirculares verticales se modificó. Las características de la respuesta pueden explicarse por la proyección de los canales anterior y posterior hacia los músculos rectos verticales y oblicuos. El cambio proporcional de la activación de cada uno de los canales semicirculares, derecho e izquierdo, se vio reflejado en la diferente combinación de las acciones primaria y secundaria de los músculos extraoculares en cada posición.

La oscilación con flexión o extensión del cuello mostró asociación entre la posición de la cabeza (en el plano sagital) con el componente horizontal de la respuesta. Lo que se puede explicar por los cambios en la posición de los canales semicirculares horizontales con respecto al plano de la oscilación en rol.

Los resultados de este estudio muestran algunos aspectos de la respuesta binocular humana a los movimientos en rol, especialmente la contribución de los canales semicirculares verticales para las características del componente vertical disconjugado.

Otolith and Semicircular Canal Contributions to the Human Binocular Response to Roll Oscillation

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Jáuregui-Renaud K, Faldon M, Clarke AH, Bronstein AM, Gresty MA. Otolith and semicircular canal contributions to the human binocular response to roll oscillation. *Acta Otolaryngol (Stockh)* 1998; 118: 170-176.

Three normal human subjects were oscillated about their naso-occipital axis in a supine position at 0.4 Hz and 0.1 Hz, both in darkness and in the light with a structured fixation target. The same subjects were oscillated in roll about an upright position, at the same frequencies, in darkness; and also about axes directed 20° and 40° to the left and to the right of the midsagittal plane, at 0.4 Hz, in darkness. Three-dimensional binocular eye movements were recorded using video-oculography. All stimuli induced a predominantly torsional nystagmus with small disconjugate head-vertical (skew) and conjugate head-horizontal components. For roll oscillation, the torsional slow phase velocity gain was higher in the light and generally increased with the stimulation frequency. In darkness, only one subject had significantly higher torsional gains in the upright compared to the supine position (12% difference), suggesting that the otolith contribution to the roll response is minimal at the frequencies tested. The slow phase velocity gain of the skew increased with fixation in two subjects, but decreased in the third subject; these changes were related to changes in eye vergence. In the upright position, with oblique axes of rotation, the head-vertical eye movements were asymmetrical, with the outermost eye executing a larger amplitude movement. The disconjugate head-vertical eye movements observed can be explained by the pattern of vertical semicircular canal stimulation and their connections to the extraocular muscles. In humans, skewing of the eyes may compensate for the eccentricity of the foveae which lie in the temporal retina and undergo vertical translations in opposite directions when the eyes turn. *Key words:* vertical semicircular canals, skew, video-oculography.

INTRODUCTION

The slow phase vestibulo-ocular response (VOR) to head movement about any axis is an eye movement in a compensatory direction (1). In humans, rotation of the head in the frontal plane (roll) provokes mainly ocular counter-rolling (2) with small disconjugate head-vertical eye movements ("skewing") (3). The response to roll has a component due to activation of the semicircular canals by angular acceleration (2) and a component induced by reorientation of the otoliths to the gravity vector (4). No otolith contribution to the slow phase VOR during passive roll motion has been shown at frequencies above 0.3 Hz (5). However, since the otoliths can detect low-frequency and static changes in head position relative to gravity (6, 7) they may be expected to make a more significant contribution to the VOR during lower frequency roll about the upright. To assess semicircular canal and otolith contributions to the human binocular response to roll motion, subjects were oscillated about both upright (variable otolith input) and supine (constant otolith input) positions, at frequencies of 0.4 Hz and 0.1 Hz, in darkness. (These procedures are described in Experiment 1).

Since the torsional VOR gain is enhanced by the presence of earth-fixed visual targets (2), it may be expected that visual feedback can also influence the disconjugate vertical component of the roll response. This effect was examined by comparing supine roll responses in darkness with those obtained in the

light, while subjects viewed a structured fixation target (Experiment 2).

One would predict from the organization of the projections of the semicircular canals to the extraocular muscles that roll stimuli may provoke a small skewing movement (3) in addition to the dominant torsional response. In order to search for further evidence of the canal origins of these disconjugate eye movements, stimuli combining both pitch and roll components of motion were used to produce a range of activation patterns for the four vertical semicircular canals (Experiment 3).

METHODS

Subjects

Three normal subjects (S1-S3) took part in the study (age range 25-30 years; one man and two women). In our experience, many normal subjects have a spontaneous vertical nystagmus (up- or down-beating) in darkness, when supine, which would obscure the effects that we wished to observe. Accordingly, the subjects of this study had minimal spontaneous nystagmus, with slow phase velocities less than 0.3°/sec. None had oculomotor abnormalities or marked phorias, but two had refractive errors (-1.25R, -1.50L, and +1R, -0.75L). All subjects gave their informed consent, according to the guidelines of the local ethics committee.

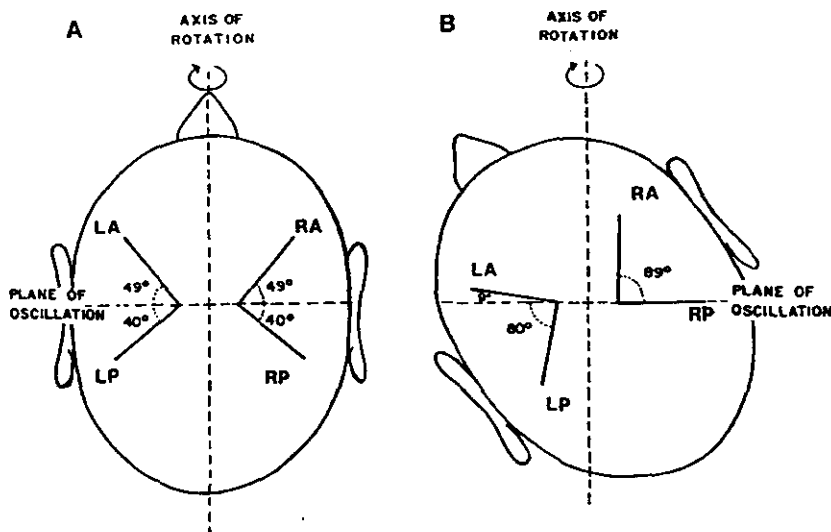


Fig. 1. Orientation of the vertical semicircular canals (view from above) during (A) oscillation about a naso-occipital axis and (B) oscillation with the nose pointing 40° to the left of the rotation axis (9). RA, right anterior; RP, right posterior; LA, left anterior; LP, left posterior.

Experiment 1: Upright vs supine oscillation, in darkness

The subjects were mounted either in gimbals with a horizontal rotation axis (upright oscillation) or on a rotating couch with a vertical rotation axis (supine oscillation), with their heads and trunks restrained. The gimbals and rotating couch were manually driven to generate whole body oscillation about the naso-occipital axis. The stimuli were quasi-sinusoidal roll oscillations, in darkness, at 0.4 Hz and 0.1 Hz, with peak velocities of $67.7 \pm 8.1^\circ/\text{sec}$ (mean \pm SD) and $27.0 \pm 4.7^\circ/\text{sec}$, respectively, about upright, and $72.3 \pm 4.7^\circ/\text{sec}$ and $25.2 \pm 3.1^\circ/\text{sec}$ when supine. The variability of head position in the sagittal plane, over all conditions, was less than 12°, as documented by photographs of the orientations of the head with respect to earth-vertical and earth-horizontal.

Supplementary experiment: Horizontal canal stimulation

During both upright and supine oscillations conjugate head-horizontal eye movements were observed, which could have been due to stimulation of the horizontal canals, if the horizontal canal plane was not orthogonal to the plane of oscillation. In order to

investigate the origin of these head-horizontal eye movements, subject S1 was oscillated in roll in the supine position, with different pitch angles of the head, i.e. with the horizontal canal plane at different orientations to the rotation axis (at 0.4 Hz, $63 \pm 2.5^\circ/\text{sec}$ peak velocity, in the dark). By flexing or extending the neck, the Reid line was positioned at 23° (forwards) or 6° (forwards) or -12° (backwards) to the earth-vertical axis of rotation.

Experiment 2: Darkness vs fixation, supine

In the supine position, subjects were oscillated in room light with an earth-stationary, structured fixation target at a distance of 42 cm. The target was a rectangular picture of a forest scene, subtending 41° by 35° at the eye; subjects were instructed to fixate a point at the centre of the target. The stimuli were roll oscillations at 0.4 Hz and 0.1 Hz, with peak velocities of $76.1 \pm 5.4^\circ/\text{sec}$ and $26.5 \pm 3.1^\circ/\text{sec}$, respectively.

Experiment 3: Oblique oscillations

Subjects were oscillated in darkness about "oblique" earth-horizontal axes, oriented 20° and 40° to either side of the midsagittal plane (i.e. nose pointing 20° or 40° to the right or to the left of the rotation axis, Fig. 1), at 0.4 Hz and $70 \pm 6^\circ/\text{sec}$ peak velocity.

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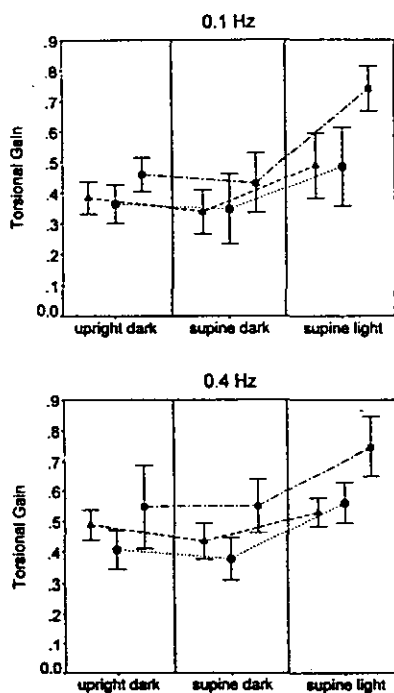


Fig. 3. Mean torsional eye movement gains for each subject. ▲, S1; ●, S2; ■, S3. Bars indicate ± 1 SD.

tion, with the head held "naturally" (Reid line 6° forward), the horizontal gain for subject S1 was 0.06; the horizontal gain was higher (0.09) during rotation with the head tilted backward (Reid line -12°). When the head was flexed into the 23° forward position, head-horizontal eye movements were less consistently related to the roll stimulus and occasionally reversed in direction. This could be due to minimal activation of the horizontal semicircular canals, assuming that, in the flexed forward position, the plane of the horizontal semicircular canals was almost perpendicular to the plane of oscillation.

Experiment 2: Darkness vs fixation, supine

Torsional eye movements. All subjects had increased torsional gain when viewing the fixation target (Fig. 3), with a mean increase of 43%. Torsional gains also increased with frequency, except for subject S3 in the light, who had a high gain of 0.74 at 0.1 Hz, and 0.75 at 0.4 Hz.

Vertical eye movements. ANOVA showed that subjects S1 and S2 both had increased skew gains with fixation, but subject S3 had a reduced skew gain in the light, which was only significant at 0.4 Hz ($p < 0.001$, *t*-test; Fig. 4). To investigate this effect, the change in vergence of each subject's eyes was measured between conditions of darkness and light. The mean horizontal position of each eye, relative to the head-fixed camera co-ordinates, was measured for each trial, and compared to the eye positions at a known vergence angle, such as during the calibration. The change in skew gain with fixation vs the change in vergence is shown in Fig. 5; positive changes in vergence indicate more convergence in the light. It seems that the magnitude of the skew is related to the degree of vergence of the eyes. Subject S3 was more convergent in the dark than in the light, which could explain the higher skew gain observed in the dark.

Experiment 3: Oblique oscillations

Vertical eye movements. Oscillation about upright, with the rotation axis orientated to the right or to the left of the midsagittal plane, evoked disconjugate head-vertical eye movements; with the rotation axis positioned between the nose and the left ear ("nose right"), the vertical movements of the right eye were larger and faster than those of the left eye, and vice versa (Fig. 6). The direction of the skew remained the same; in the "nose right" position, for positive stimuli (pitch component forward, roll component to the right), both eyes had slow phases upwards, but the intorting right eye moved upwards more quickly than the extorting left eye. In the "nose left" position, for positive stimuli (pitch component backward, roll component to the right), both eyes had slow phases downwards, but the intorting right eye moved downwards more slowly than the extorting left eye. The skew gain decreased with the eccentricity of the rotation axis, as expected when the proportion of stimulation in the frontal plane was reduced (Fig. 7).

DISCUSSION

The torsional eye movement gains observed are in agreement with previous studies in which human subjects were exposed to low-frequency oscillation in darkness (5). Small differences in gain, related to the orientation of the rotation axis with respect to gravity, were seen in one subject; but the results indicate that the otolith contribution to the torsional roll response is functionally insignificant at the frequencies tested.

The occurrence of disconjugate vertical eye movements during both upright and supine roll motion confirms that, in normal man, skewing eye move-

Eye movement recording

Binocular, three-dimensional eye movement recordings were obtained using computerized video-oculography (VOG: SMI, Berlin) (8). Video images of each eye were obtained with two cameras mounted on a SCUBA diving mask, which was further secured to the head with a bite board. The recordings were processed off-line to give head-horizontal and head-vertical eye movements at a sampling rate of 50 Hz, and torsion about the centroid of the pupil at a sampling rate of 25 Hz. During experiments subjects were instructed to look straight ahead. A control experiment was performed to quantify possible artefacts from displacement of the cameras during the oscillation: Experiment 1 was reproduced on one subject, whose eyes were covered with white patches with black dots at the approximate position of the eyes. Recordings from these simulated eyes showed occasional displacement of the cameras during oscillation about upright (u) and supine (s); the largest displacements observed were: 2° (u) and 0.4° (s) in the head horizontal plane and 1.5° (u) and 0.4° (s) in the head-vertical plane.

Analysis of oscillation data

For each condition, oculomotor responses and stimuli were measured on 10–16 cycles. The gimbals or couch position was transduced using a potentiometer, then the peak stimulus velocity in each cycle was found from the differentiated position trace (two-point central difference algorithm). The eye velocity was measured from the slope of the nystagmus slow phases, as the low sampling rate and frequent nystagmus beats made measurements from differentiated eye position traces difficult. Torsional gain was defined as the ratio of peak torsional slow phase eye velocity to peak stimulus velocity. The ocular skew was found by subtracting the vertical position of the left eye from the vertical position of the right eye; skew gain was defined as the ratio of peak slow phase skew velocity to peak stimulus velocity. Intra-individual comparisons of torsional and skew gains for different body orientations, oscillation frequencies and fixation conditions were analysed using analysis of variance (ANOVA), followed by *t*-tests for independent samples, where significance was found (CSS Statistica; significance taken as $p < 0.05$).

RESULTS

Both upright and supine oscillation provoked a predominantly torsional nystagmus, with slow phase velocity partly compensatory for the stimulus velocity. In addition, small conjugate head-horizontal and disconjugate head-vertical eye movements were observed

which were systematically related to the stimulus (Fig. 2). The eye with the extorting slow phases moved downwards whilst the eye with the intorting slow phases moved upwards.

Experiment 1: Upright vs supine oscillation, in darkness

Torsional eye movements. Torsional gains are plotted in Fig. 3. There was a trend for higher torsional gains in the upright position, but only one subject showed a statistically significant difference in torsional response when comparing upright and supine oscillations, with a 12% increase in gain for roll about upright (at both 0.4 Hz and 0.1 Hz; $p < 0.02$, *t*-test).

Vertical eye movements. Skew gains are plotted in Fig. 4. At 0.4 Hz, two subjects (S1 and S2) had significantly higher skew gains in the upright position ($p < 0.001$, *t*-test). This could indicate an otolith contribution to the skew response at 0.4 Hz.

Supplementary experiment: Horizontal canal stimulation

Horizontal eye movements. Under most conditions, roll motion to the right evoked horizontal slow phase movements to the left (and vice versa). Since the plane of the horizontal semicircular canals is not orthogonal to the frontal plane (9), roll stimulation in the frontal plane would stimulate the horizontal canals, with an expected response in the observed direction. A horizontal eye movement gain was defined as the ratio of peak horizontal slow phase eye velocity to peak stimulus velocity. In the supine posi-

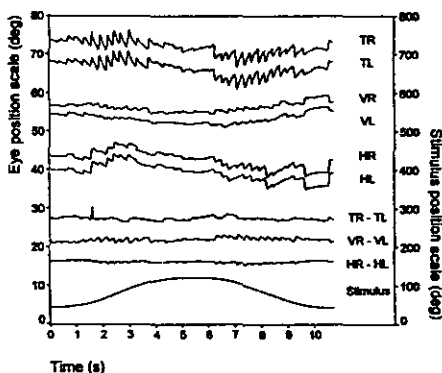


Fig. 2. VOG eye movement recordings from subject S3, during one cycle of supine oscillation in the light, at 0.1 Hz. Increasing signals indicate dextrotorsion (T), upwards vertical (V) and rightwards horizontal (H) movements, of the right (R) and left (L) eyes. Skewing is seen clearly in the difference trace (VR-VL).

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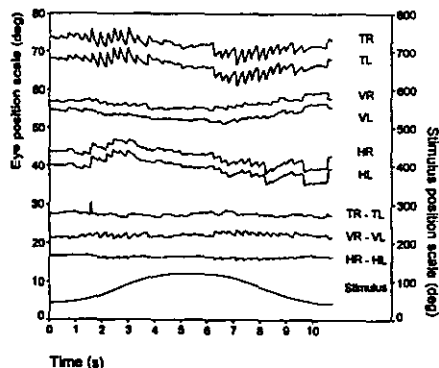


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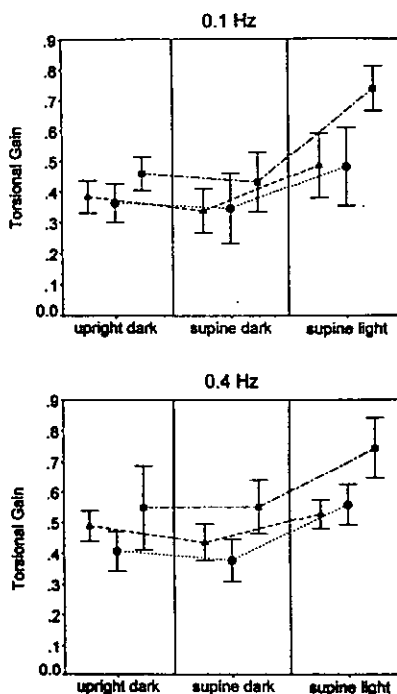


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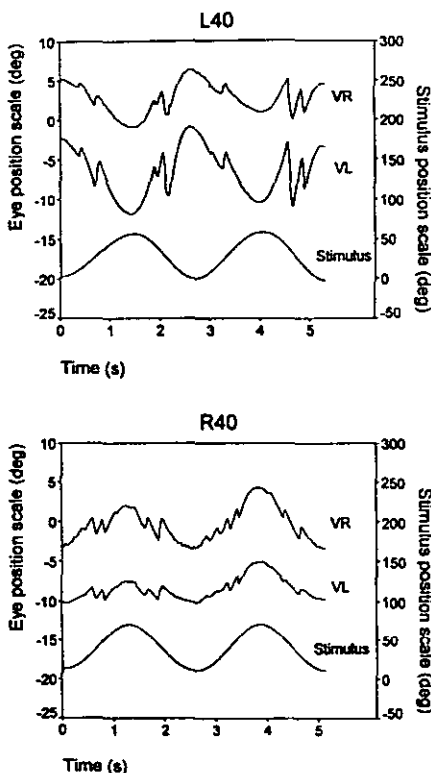


Fig. 6. Vertical eye movements, from subject S1, during oblique oscillations. L40, 40° nose left; R40, 40° nose right; VR, right eye; VL, left eye. Increasing signals indicate upwards eye movements. (The head orientation for L40 is illustrated in Fig. 1B.)

visual axis are not the same. The fovea is displaced towards the temporal field of the retina, with respect to the optical axis, by a variable angle of about 5° (16, 17). Thus, if the eyes tort about their optical axis, the fovea of the intorting eye will move up, whereas that of the extorting eye will move down. To compensate for this retinal misalignment the intorting eye must rotate upwards and the extorting eye must rotate downwards, which is exactly what happens during the slow phase of the skewing nystagmus. This hypothesis is in agreement with the apparent enhancement of the skew with vergence seen in Experiment 2, and also reported for static tilt in normal human subjects using red-green dissociation of the

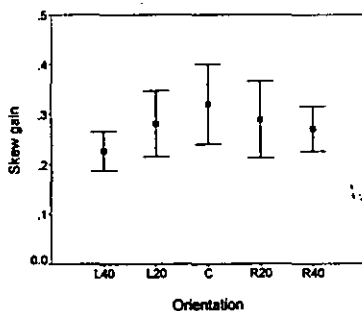


Fig. 7. Variation in mean skew gain with the eccentricity of the rotation axis, for subject S3. L40 (L20), 40° (20°) nose left; R40 (R20), 40° (20°) nose right; C, centred. Bars indicate ± 1 SD.

eyes (18). As the eyes converge, the angle between the (head-fixed) axis of rotation and the visual axis of each eye will increase, requiring a larger vertical movement to compensate for the increased misalignment of the foveae. Further experiments are required to investigate the function of the skew more fully.

The finding of vertical disconjugacy of the eyes, in normal human subjects, due to semicircular canal activation extends our concepts of the possible origin of "pathological skewing", by suggesting that it may be attributable not only to lesions of the otolith pathways (19) but also to lesions of the oculomotor pathways related to vertical semicircular canal function.

ACKNOWLEDGEMENTS

This work was supported by grants from CEC Biomed Concerted Action BMHI CT94 and CEC Access to Large Scale Facilities ERB CHGE CT93 0020. K.J.-R. was supported by a grant from the Mexican Social Security Institute.

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ments can be evoked by vertical semicircular canal stimulation (3). Further insight into the vertical canal contribution to eye movement control comes from the results of the oscillation about oblique axes. During roll oscillation about a naso-occipital axis, there is an alternating co-activation of the right anterior and posterior and the left anterior and posterior semicircular canal pairs (Fig. 1A). The principal excitatory connections from each semicircular canal to specific extraocular muscles (10, 11) will produce activity of oblique and vertical recti muscles, which generate not only eye torsion but also a vertical misalignment (12), since the action of the recti is stronger (13).

During oscillation about oblique axes the pattern of activation and inhibition of the anterior and posterior semicircular canals is modified. For example, assuming that the orientations of the anterior and posterior semicircular canals with respect to the frontal plane are about 49° and 40° , respectively (9),

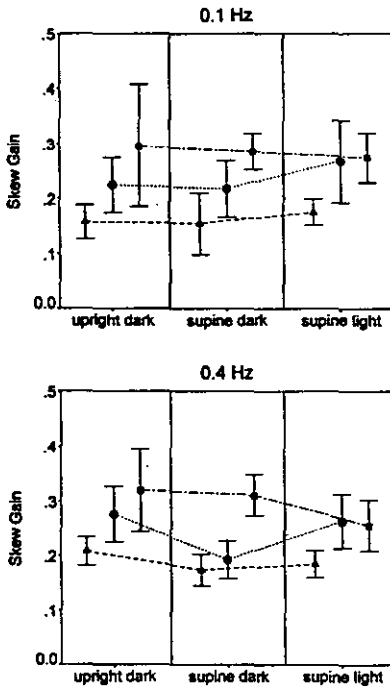


Fig. 4. Mean skew gains for each subject. ▲, S1; ●, S2; ■, S3. Bars indicate ± 1 SD.

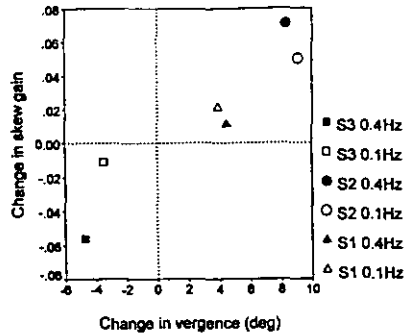


Fig. 5. Change in skew gain with fixation for each subject vs changes in vergence. Positive values indicate more convergence, and higher skew gains, in the light.

oscillation of a subject about an axis with nose 40° left would alternately activate the right posterior canal (with almost no activation of the right anterior canal) and the left anterior canal (with a small activation of the left posterior canal) (Fig. 1B). Our results show that this stimulus produces an asymmetric vertical deviation of the eyes, with a larger displacement of the left eye than the right eye, which can be explained by the connections between the activated semicircular canals and the extraocular muscles. For roll to the right shoulder, the primary vestibular projection would be a main excitatory input to the right superior oblique and the left inferior recti muscles, with almost no input to the right superior recti and the left inferior oblique muscles. The primary and secondary actions of these muscles (14) would produce laevotorsion and asymmetrical depression of the eyes, with a larger vertical movement of the left eye. For roll to the left shoulder, the main canal input to the left superior rectus and the right inferior oblique muscles and the small input to the left superior oblique and the right inferior recti would produce dextrotorsion and asymmetrical elevation of the eyes, again with a larger vertical movement of the left eye. The inverse is the case for oscillation about an axis with nose 40° right.

Why roll motion should induce skewing of the eyes in normal human subjects is not clear, as it would potentially create vertical diplopia. One explanation is that skewing could be vestigial, a remnant of the realignment of the visual streaks to the horizon that animals with laterally positioned eyes show during roll motion (15).

An alternative view is that the skew has a useful function. The axis of rotation of the globe and the

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Submitted December 13, 1996; accepted June 2, 1997

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ETAPA II

Documento en referencia al final del capítulo. Se ha solicitado una publicación en *Experimental Brain Research*, con resultados preliminares en: *J Physiol* 1997;505P: 78-9.

La vergencia ocular horizontal y la respuesta tridimensional a los movimientos en rol

La divergencia vertical de los ojos, registrada mediante video-oculografía, como parte de la respuesta oculomotora a un estímulo dinámico en rol, debía ser confirmada con especial atención a la presencia de posibles artefactos durante la rotación y el registro oculomotor. La posible influencia de la vergencia horizontal en las características de la respuesta vestibulo-ocular en este plano podría contribuir a comprender mejor este fenómeno.

Objetivos

Identificar las características del componente vertical de la respuesta vestibulo-oculomotora binocular humana a los movimientos de todo el cuerpo en rol (peri-rotatoria y post-rotatoria), cuando se estimula a los canales semicirculares verticales de forma dinámica y a los otolitos de forma constante y se registra mediante la técnica de localización magnética, y su posible modulación por el ángulo de convergencia horizontal de los ojos.

Metodología

Seis sujetos jóvenes, de 23 a 36 años (3 mujeres), sin evidencia de alteraciones neuro-otológicas o de los movimientos oculares aceptaron participar en el estudio. Previa calibración *in vitro* de los 'coils' sensores, en posición decúbito supino, con el eje naso-occipital orientado verticalmente sobre el pivote de una mesa para rotación manual, con el cuerpo sujeto a la

mesa y la cabeza sujeta al centro de un campo magnético, se efectuó calibración *in vivo* de los sensores y se realizaron los siguientes procedimientos.

- Rotación de todo el cuerpo alrededor del eje naso-occipital del sujeto, a velocidad media de $56.5 \pm 3.1^\circ/\text{s}$ durante 40 segundos, en la oscuridad, hacia la derecha y después hacia la izquierda, con detención súbita y registro oculomotor durante y por al menos 30 segundos después de la rotación.
- Oscilación quasi-sinusoide de todo el cuerpo, alrededor del eje naso-occipital del sujeto, aproximadamente a 0.4 Hz ($69.1 \pm 3.9^\circ/\text{s}$), durante un minuto y en tres ocasiones, cada una con un descanso intermedio: 1) en la oscuridad; con fijación visual en un punto único generado por un LED localizado a una distancia aproximada de 2) 2.06 m y 3) 0.47 m.

Los movimientos de los ojos y de la cabeza fueron registrados mediante la señales de 'coils' sensores montados en anillos esclerales (Skalar, Delft), a un índice de muestreo de 500 Hz. El movimiento de la mesa se registró utilizando un potenciómetro pre-calibrado. Se calculó la velocidad angular del ojo en un sistema ortogonal de coordenadas fijas a la cabeza (W_x , W_y y W_z), en el que los valores positivos corresponden a rotaciones dextro-torsionales, hacia la izquierda y hacia abajo. El sistema de coordenadas de Fick, fijas a la cabeza, se eligió para describir la posición ocular, por el orden en que se especifican cada uno de los componentes (Figura 1).

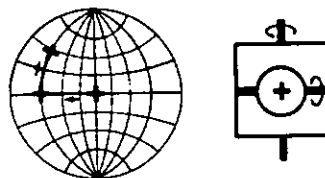


Figura 1. Sistema de Fick, el componente horizontal se especifica primero, después el vertical y por último el de torsión.

El componente vertical se estudió en cada ojo y en el trazo obtenido de sustraer el registro del ojo izquierdo del registro del ojo derecho. La ganancia de velocidad se calculó por la pendiente de la línea de regresión entre la velocidad de fase lenta del nistagmus vs la velocidad del estímulo.

Las constantes de tiempo del decaimiento de las respuestas post-rotatorias se calcularon en el perfil de decaimiento exponencial de la velocidad media de cada batida nistágmica; para estas respuestas se calculó la ganancia de velocidad como la proporción que resulta de dividir la velocidad máxima de la fase lenta de la respuesta post-rotatoria entre la velocidad del estímulo durante la rotación.

Resultados y Comentarios

FASE LENTA DEL NISTAGMUS

Los componentes de torsión y horizontal de la respuesta (peri-rotatoria y post-rotatoria) fueron conjugados y el componente vertical fue disconjugado, tanto en la obscuridad como con fijación visual. La dirección de los ejes de rotación de cada ojo en el plano transversal, calculados a partir de los componentes de torsión y vertical, se encontró asociada a la posición ocular horizontal.

Los ejes de rotación de los ojos no estuvieron alineados con el eje de rotación de la cabeza (estímulo), y durante la fijación visual su convergencia fue aún mayor de lo esperado por la posición del punto de fijación. Hallazgo que es congruente con los informes acerca de que la posición primaria del ojo (definida por el plano de Listing) está en exo-desviación ocular y no tiene una orientación fija a la cabeza (Bruno 1997).

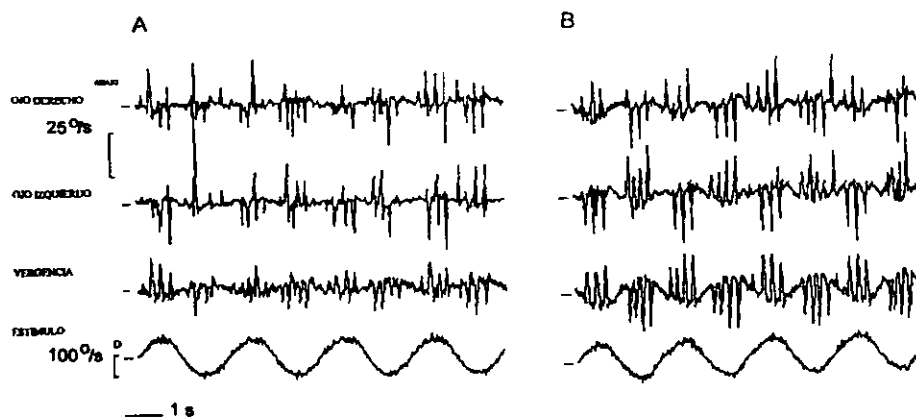


Figura 2. Componente vertical de la velocidad angular de los ojos durante la oscilación en rol con fijación visual en un punto único lejano (A) y en un punto único cercano (B).

La ganancia de velocidad de torsión y del componente vertical disociado fue diferente al cambiar el grado de convergencia horizontal (Figura 2). La fijación visual en un punto único cercano se asoció a mayor ganancia de torsión y menor ganancia vertical para todos los sujetos ($p < 0.05$, Prueba de Rangos con Signo de Wilcoxon).

Cuando los ojos se mueven, la menor o mayor ganancia de cada uno de los componentes de la velocidad ocular depende de la fuerza relativa y planos de acción de los músculos extra-oculares. Los puntos de inserción funcional de estos músculos se encuentran fijos a la órbita (Demer 1995). Por estos motivos, cuando la cabeza se mueve, para que se lleven a cabo movimientos oculares compensatorios apropiados es necesario considerar la posición del ojo en relación a la cabeza. Cambios en la inervación de cada uno de los músculos participantes contribuyen a lograr el balance adecuado entre las acciones de los músculos necesarios para cada movimiento compensatorio.

Después de rotación a velocidad continua en la obscuridad, la ganancia del componente de torsión fue de 0.39 ± 0.06 y del componente vertical disociado fue de 0.08 ± 0.03 . El decaimiento de la velocidad de la respuesta fue de $4.5 \pm 1.5s$ y $5.8 \pm 1.9s$ respectivamente. Lo que confirma la evidencia previa de que para la respuesta vestibulo-oculomotora que involucra principalmente a los canales semicirculares verticales, existe mínima o nula memoria de velocidad, y por lo tanto está determinada principalmente por las características del laberinto (ver Apéndice).

FASE RAPIDA DEL NISTAGMUS

Los perfiles de velocidad de los componentes de torsión y horizontal de cada ojo fueron simétricos, los del componente vertical fueron asimétricos y lentos. La dirección de los ejes de rotación durante la fase rápida de la respuesta fueron similares a los observados para la fase lenta.

La fase rápida del nistagmus es un movimiento de re-fijación que no se encuentra controlado por el estímulo vestibular y sus componentes tridimensionales están inter-relacionados (Crawford 1991b).

Durante la fase rápida del nistagmus a los movimientos en rol, los componentes verticales se efectúan junto a componentes de torsión amplios que requieren de la contracción simultánea de los músculos oblicuo superior y recto superior de un ojo y oblicuo inferior y recto inferior del ojo contra-lateral. Pares de músculos que tienen acción de torsión sinérgica pero acción vertical en dirección opuesta. Este hecho podría explicar las características oscilatorias del perfil de velocidad del componente vertical identificadas en el estudio.

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HORIZONTAL OCULAR VERGENCE AND THE 3D RESPONSE TO ROLL MOTION

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SUMMARY

To evaluate the human binocular response to roll motion in the dark and during visual fixation with horizontal convergence, six normal human subjects were exposed to manually driven, whole-body rotation about an earth-vertical, naso-occipital axis, under two conditions: I. Oscillation at 0.4Hz (69°/s, S.D. 3.8°/s) in the dark, and while fixating an axial LED at 47cm (near) and at 206cm (far); II. Constant velocity rotation (56.5°/s, S.D. 3.1°/s) for 40s, clockwise and counter-clockwise, in the dark. Eye and head movements were monitored using scleral search coils. Roll motion always evoked conjugate ocular torsion, with small conjugate horizontal and disconjugate vertical velocity components. The resultant binocular eye responses were rotations about convergent axes. During oscillation with target fixation the convergence of the rotation axes was larger than that predicted by target geometry, producing disconjugate vertical gaze oscillations about the target ('skewing'). In response to velocity steps, eye velocity decayed exponentially with time constants of 4.5s (S.D. 1.5s) for the torsional component and 5.8s (S.D. 1.9s) for the 'vertical vergence' component (right eye - left eye recordings). Fast phase eye movements with large torsional angular velocities had vertical velocity components with complex and asymmetrical profiles. This finding could be explained by the antagonistic vertical action of the yoking pair of muscles which are needed to execute torsional eye movements. We conclude that in normal human subjects dynamic vertical canal stimulation, with horizontal gaze convergence, evokes rotation of the eyes about convergent axes, and skewing of the eyes. The response to roll motion, both with and without fixation, is modified by the horizontal ocular vergence.

Key words: Human, Vestibulo-ocular reflex, Semicircular canals, Head roll

INTRODUCTION

In normal man, rotations of the head in the frontal plane (roll) evoke not only ocular counter-rolling (Collewijn 1985) but also small disconjugate head-vertical and conjugate head-horizontal eye movements (Jáuregui-Renaud 1996). Vertical disconjugacy of the eyes has also been observed in some patients with unilateral vestibular lesions. It has been proposed that this vertical disconjugacy could be mediated by the otolithic vestibular pathways (Wolfe 1993) or by a combination of otolithic and semicircular canal pathways (Brandt 1993). However, in normal man, vertical disconjugacy can be evoked with pure semicircular canal stimulation during roll motion about an earth-vertical axis (Jáuregui-Renaud 1998), when otolithic stimulation is constant. The current work investigates further the nature of the three dimensional (3D) binocular response to roll oscillation and the stopping responses to roll velocity steps.

The reason why an apparent vertical disconjugacy of the eyes should be induced by roll stimuli is not clear. During movements of the head, the vestibulo-ocular reflex (VOR) acts to maintain a stable position of the eyes in space. To prevent image slippage on the retina, rotation of the head in the frontal plane, while the subject looks straight ahead (to a target at infinity), requires a compensatory rotation of the eye about an axis parallel to the roll axis of the head. However, with gaze convergence on a nearer, axial target, maintenance of fixation requires eye rotation about an axis which is not parallel to the axis of head rotation (Fig. 1A). If the eyes rotated about their convergent gaze directions, then the eye velocities would comprise conjugate torsional components, and head-vertical components in opposite directions for the two eyes. In this case, the disconjugacy of the vertical components could be related to the gaze directions of the eyes. In order to study how binocular visual fixation, with near and far horizontal convergence, affects the 3D characteristics of the response to roll stimuli, we oscillated subjects in the dark and with axial fixation targets at two different distances. Preliminary results have been reported in abstract form (Jáuregui-Renaud 1997).

MATERIAL AND METHODS

Subjects.

Six normal human subjects (3 female), 23 to 36 years old, gave their consent to participate in the study. None of them had prior history of neurological or otological disease. Three of them were myopes and habitually wore refractive correction, which was not used during the experiments. Subjects lay supine on a rotating couch, with their head aligned such that the axis of rotation passed between the eyes; the head was fixed to the couch using head clamps and the trunk was firmly restrained by adjustable belts. Variation of the head position in the sagittal plane, measured by the Reid's line, was less than 12°, between subjects; for each subject, the angle between the Reid's line and the earth-vertical was equal or less than 22°.

Stimuli.

1. The subjects were exposed to manually driven, approximately sinusoidal oscillation of the whole body about the naso-occipital axis at 0.4 Hz, 69°/s peak velocity (S.D. 4°/s) in three consecutive conditions: 1) in darkness, 2) with visual fixation on a single LED, centred at 47 cm from the eyes ('near' target), in an

otherwise dark room and 3) with visual fixation on an LED at a distance of 206 cm from the eyes (far target), in an otherwise dark room.

The mean horizontal gaze convergence required by the target geometry was 7.6° for the near target and 1.8° for the far target. In Fick co-ordinates, the actual mean convergence with fixation on the near target was 7.5° (S.D. 0.6°) and with fixation on the far target was 1.5° (S.D. 0.4°).

ii. To study stopping responses, all the subjects were also exposed to 40s of constant velocity rotation at $56.5^\circ/\text{s}$ (S.D. $3.1^\circ/\text{s}$), clockwise and counter-clockwise, in the dark.

Motion of the couch was transduced with a potentiometer.

Eye movement recording.

Binocular eye movements were measured in three dimensions, using a scleral coil system. The field coils (70cm cube, CNC Engineering, Seattle) were mounted on the rotating couch and moved with the subject. Eye and head movements (relative to the field coils) were recorded using combination scleral coils supplied by Skalar, Delft. Movements of the head were monitored with a coil mounted on the subject's forehead. Signals from the coils were sampled at a rate of 500 Hz.

Data processing.

The search coil signals were analysed off-line to estimate the angular velocity of the eye globe (Merfeld 1992), and the eye position (Ferman 1987, Robinson 1983).

Angular velocity

The angular velocity of the eye globe was expressed in orthogonal, head-fixed co-ordinates, to allow vector summation and comparison of the net angular velocity with the stimulus. We used a 'right-handed' co-ordinate system, with the x-axis pointing straight ahead, the y-axis lying on the inter-aural axis, pointing leftward, and the z-axis along the longitudinal axis, pointing through the top of the head (Fig. 1B). Torsional angular velocity is defined as the component of the angular velocity about the x-axis, with positive velocities when the top of the eye is moving to the right shoulder; vertical angular velocities, about the y-axis, are positive for downward movements; and horizontal angular velocities, about the z-axis, are positive for leftward movements (right-hand rule).

Eye position

Eye position was expressed in Fick co-ordinates. The Fick co-ordinate system has 'nested' axes: from a reference position, with gaze straight ahead, an eye displacement is expressed in terms of a horizontal rotation, followed by a vertical rotation (about an axis orthogonal to the gaze direction), followed by a torsional rotation about the final gaze direction. These co-ordinates are well suited to our experiment, because the horizontal eye position is established by the target location; then we are interested in the vertical gaze direction, which is not affected by torsion about the line of sight.

Eye velocity gain

The gain of the torsional component of the response was given by the slope of the linear regression of torsional slow phase eye velocity versus stimulus velocity (with the optimum phase shift). A value for 'vertical gain' was found by subtracting the vertical angular velocity of the left eye from that of the right eye (RE-LE), and calculating the slope of the linear regression of this trace against the stimulus velocity.

Time constants

Time constants of the stopping responses were measured from the angular velocity traces. The mean slow phase velocity and time of each nystagmus beat were determined. To find the time constant, an exponential profile was fitted to the slow phase beat data preceding the time when the total angular velocity had decayed to 10% of its peak value. Response gain was defined as the ratio of the peak slow phase eye velocity to the steady state stimulus velocity.

RESULTS

Roll stimulation provoked a 3D vestibular nystagmus with slow and fast phases.

The main element of the slow phase response was a conjugate torsional rotation in the opposite direction to the stimulus, with accompanying small conjugate horizontal and disconjugate vertical components. The fast phases reset the eyes via movements with conjugate torsional and horizontal components and asymmetrical vertical components.

SLOW PHASE RESPONSE TO SINUSOIDAL OSCILLATION

Rotation axis convergence.

The angular velocity profiles of the slow phase response were conjugate for the torsional and horizontal components and disconjugate for the vertical components (Fig. 2). A plot of the torsional component of the angular velocity against the vertical component gave the instantaneous rotation axis of each eye in the transverse plane. Since these components were well correlated, the direction of the net rotation axis of each eye was fairly constant during the roll oscillation (Fig. 3).

During roll with visual fixation the rotation axes of the two eyes were convergent; with the convergence due to the disconjugate nature of the vertical angular velocity components. In order to measure the degree of rotation axis convergence, a regression line was fitted (through the origin) to the plot of torsional against vertical angular velocity, using a least-squares method (to minimize the sum of orthogonal distances of each data point to the regression line) [see Appendix]. The rotation axis convergence for each subject, under both fixation conditions, is given in Table 1. The rotation axis convergence was greater than the measured gaze convergence in 5 out of 6 subjects, producing disconjugate oscillations of the vertical gaze directions of the two eyes ('skewing') (Fig. 4).

During roll in the dark, without a fixation target, horizontal eye vergence was variable. However, for each subject, a plot of the convergence of the eye rotation axes (in the transverse plane) versus the convergence

of the horizontal gaze, for each half-cycle of oscillation, showed that the rotation axis convergence in the dark depended on the measured horizontal gaze convergence in proportion to the values obtained with the fixation targets (Fig. 5).

Eye Velocity Gains

The mean gain of the torsional angular velocity component in the dark was 0.37 (inter-subject range from 0.22 to 0.52); for visual fixation on the near target it was 0.31 (0.17 to 0.47) and for visual fixation on the far target the mean torsional gain was 0.38 (0.28 to 0.50). The mean gain of the vertical component (RE-LE) in the dark was 0.06 (0.02 to 0.13); for the near target it was 0.06 (0.04 to 0.1) and for the far target the mean vertical gain was 0.04 (0.02 to 0.1). Torsional gain during fixation on the near target was 20% lower than that for fixation on the far target (change of 0.07 ± 0.03 S.D.); whereas the vertical gain was 40% higher during fixation of the near target (change of 0.02 ± 0.01 S.D.) (Fig. 6). Vector summation of these torsional and vertical velocity gains, to indicate the effective eye rotation axes, reflects the increased rotation axis convergence during near as opposed to far fixation.

SLOW PHASE RESPONSE TO VELOCITY STEPS

The stopping stimulus evoked conjugate torsional nystagmus, with the slow phase rotation in the same direction as the original roll stimulus. As during sinusoidal roll stimulation, this torsional response was associated with conjugate horizontal components and disconjugate vertical components.

The mean peak velocity of the torsional slow phase response was $22^\circ/\text{s}$ (S.D. $4^\circ/\text{s}$), which is equivalent to a 'high frequency' gain of 0.39 (S.D. 0.06). The 'vertical vergence' response was found by subtracting the vertical angular velocity of the left eye from that of the right eye. The peak slow phase velocity of this response was $4^\circ/\text{s}$ (S.D. $2^\circ/\text{s}$) (a 'high frequency' gain of 0.08 (S.D. 0.03)). The slow phase velocity profiles showed an exponential decay with time constants of 4.5s (S.D. 1.5s) for the torsional component and 5.8s (S.D. 1.9s) for the vertical vergence component (Fig. 7).

The stopping responses were measured in complete darkness, so the effective eye rotation axis was related to the measured horizontal gaze direction, to compare this data with the sinusoidal data. The instantaneous convergence of the rotation axes was found from the torsional and vertical angular velocities of each eye, during each slow phase of the nystagmus; the simultaneous horizontal gaze convergence was given by the horizontal eye position in Fick co-ordinates. A plot of rotation axis convergence versus horizontal gaze convergence shows a linear relationship, with the convergence of the rotation axes generally larger than the gaze convergence. (Fig. 8).

FAST PHASE RESPONSE

Close examination of the fast phase components of the vestibular response revealed that the characteristics of the vertical components of eye velocity were different to those of the torsional and horizontal components. Torsional and horizontal components had binocularly symmetric velocity profiles, while the

vertical components were asymmetric, with a complex and oscillatory behaviour (Fig. 9). The greatest asymmetry of the vertical angular velocity traces appeared during the first 20 ms of the fast phase.

During the fast phase response, the vertical components were slower than the torsional components (Fig 9). Torsional components of 0.8° (S.D. 0.4°) showed peak velocities of 7 to $112^\circ/\text{s}$ (mean $38^\circ/\text{s}$, S.D. $17^\circ/\text{s}$), while vertical components of similar size (0.8° , S.D. 0.3°) showed peak component velocities of 4 to $69^\circ/\text{s}$ (mean $30^\circ/\text{s}$, S.D. $12^\circ/\text{s}$) ($p < 0.00001$, 't' test).

By analogy with the slow phase data analysis, a plot of torsional fast phase angular velocity against vertical fast phase angular velocity shows the trajectory of the fast phase angular velocity vector, in the transverse plane (Fig 10). Plotted in this way, most fast phases exhibit asymmetrical, loopy trajectories. However, splitting the binocular vertical angular velocities into conjugate (see Fig. 10A, Wymean) and converse elements (see Fig. 10A, Wydiff) (see Appendix), and combining the converse vertical velocities with the torsional velocities gives steady eye rotation axes, which are convergent in the two eyes. The convergence angles of these fast phase rotation axes are very similar to the values found for the corresponding slow phase data; during sinusoidal oscillations, with near fixation, the mean difference between slow phase and fast phase rotation axis convergence is 0.6° (S.D. 2.9°), and with far fixation the mean difference is also 0.6° (S.D. 1.8°). Both up and down conjugate elements of the vertical velocities were observed during resetting movements in both directions. These elements could represent symmetrical vertical components of eye movement, occurring simultaneously with the fast phase eye rotations about the convergent axes.

DISCUSSION

SLOW PHASE RESPONSE

Sinusoidal oscillation

The results show that, during head roll, the directions of the rotation axes of the eyes (in the transverse plane) change with eye position, both in the dark and during visual fixation on an axial target. During fixation the rotation axes are steady and convergent, but the rotation axis convergence is larger than the horizontal gaze convergence. This difference between the rotation axis directions and the gaze directions produces a vertical dissociation of the eyes.

The misalignment between the axes of rotation of the eyes and the stimulus axis is in agreement with the existing evidence that the gain of the visually assisted VOR seems to be lowest about an axis parallel with the primary eye position (orthogonal to Listing's plane) (Crawford 1991). The primary eye positions of human subjects, during fixation on a far target, are generally found to be exo-deviated. However, the primary eye positions do not have a fixed orientation in the head and can be modified by the convergence state of the eyes (van Rijn 1993, Bruno 1997), with the exo-deviations being larger during convergence. If the VOR gain for each eye is minimal about axes aligned with the exo-deviated primary positions, roll stimulation with gaze convergence would produce eye rotations about convergent axes; the degree of rotation axis convergence being dependent on the relative torsional and vertical VOR gains and the exo-

deviations of the primary positions of each eye. In our experiments, the exceptionally large rotation axis convergence observed for one subject (MA) (see Table 1 and Fig 5), could be explained by the very low torsional gains of his responses (Fig 8).

In order to understand the characteristics of the VOR response to roll motion, we have to consider the oculomotor mechanisms needed to execute a torsional eye movement. When the eyes move, the spatial orientations of the rotation axes depend on the innervations, relative strengths and planes of action of the extra-ocular muscles. During roll stimuli, ocular counter-rolling is produced by the combined action of the superior rectus and superior oblique muscles of one eye and the inferior rectus and inferior oblique muscles of the contra-lateral eye. Individually, the action of these muscles induce ocular rotations which are all intermediate between the head-fixed torsional and vertical axes. During ocular counter-rolling, the resultant rotation axes of each eye lie close to the roll axis, with a convergent vertical component dependent on the relative action of the recti and oblique muscles (López 1992).

Although eye muscles have paths which are stable relative to the orbit (Demer 1995, Demer 1996)¹, our results show systematic changes in eye rotation axes with horizontal gaze convergence. This finding might be related to small movements of eye muscle insertion points (relative to the head) and the effective muscle origins (due to pulley compliance) as the eye globe rotates. However, the actions of extraocular muscles depend not only on the muscle pulling directions but also on muscle innervation. When the head is moving, the VOR has to take account of the eye position relative to the head; changes in eye position would be accompanied by changes in eye muscle innervation to keep the eye stable in space. Therefore, in our experiments, changes in muscle innervation could contribute to the changes in eye rotation axis orientation with gaze convergence.

¹Imaging studies have shown that the paths of extraocular muscles remain fixed in the orbit during large extraocular rotations and across large surgical transpositions of their insertions. This stability is due to their passage through pulleys which are coupled to the orbit and located near the equator of the globe (Demer 1995, Demer 1996).

Stopping responses.

A vertical disconjugacy of the eyes was also observed during the stopping responses. This result confirmed that pure vertical semicircular canal activation can evoke a vertical disconjugacy of the eyes.

The measured time constants of the torsional component were similar to those previously reported for human subjects rotated whilst seated on a chair with their neck hyper-extended (Seidman 1989). Results were variable among subjects, but the mean time constants were close to the estimated time constant of the human cupula (Raphan 1979). The data confirm that there is little or no velocity storage for the torsional VOR (Tweed 1994) for rotations about an earth-vertical naso-occipital axis. Under our

experimental conditions, the characteristics of both the torsional and the disconjugate vertical components of the response seem to be mainly determined by the mechanical properties of the semicircular canals.

FAST PHASE RESPONSE

The fast phases were mainly torsional with small vertical and horizontal components. The vertical velocity components had complex asymmetrical profiles.

One hypothesis is that the asymmetry of the vertical components of the fast phase could be related to vergence mechanisms. Although adjustments in vertical alignment are normally slow (Kertesz 1983), the speed of vergence can increase when the vergence movement is incorporated with a saccade (Zee 1992). However, the dynamic characteristics of the fast phases were dissimilar to previously published characteristics of vertical vergence movements. Vertical saccades with disparities have been reported with peak velocities up to 20 to 30°/s (Ygee 1995), but the greatest change of alignment was reached after the end of the saccadic pulse (up to 900 ms later). During our experiments, we observed the greatest disconjugacy of the vertical fast phase components during the first 20 ms of the eye movements. Therefore, the complex profiles of the vertical components of the fast phase, observed in our data, cannot be explained just by vergence mechanisms.

An alternative explanation for the vertical fast phase characteristics depends on the action of the extraocular muscles required to produce a mainly torsional fast phase. Saccadic control occurs for the three dimensions simultaneously (Crawford 1991), and the characteristics of the 3D components of a fast phase are interrelated. During the response to roll, the vertical components accompany large conjugate torsional components, produced by the co-contraction of the superior oblique and the superior rectus muscles of one eye and the inferior oblique and the inferior rectus muscles of the contra-lateral eye. These pairs of muscles have vertical actions in opposite directions. So, the disconjugacy and slowness of the vertical components of the fast phase response to roll could be determined by the simultaneous contraction of muscles which have a synergistic torsional action but an antagonistic vertical action.

Investigation of the complex vertical velocity components of the fast phases suggested that the profile for each eye could be divided into conjugate and converse elements (Fig 10A, Appendix). The converse vertical elements (oppositely directed in the two eyes), when combined with the torsional velocity components, produced a simple rotation about the convergent, slow phase rotation axes, but in the opposite direction to the slow phase. The conjugate vertical elements could be regarded as a conjugate vertical eye movement occurring simultaneously with the fast phase, resetting rotation about the convergent axes. The polarity of these components did not appear to be consistent and its significance is therefore unclear; they could correct for small eccentricities of the head or the fixation target.

In conclusion, our results showed that the binocular response to roll stimulation is a slow phase movement about convergent eye rotation axes, with fast phase, resetting movements in the opposite direction. During

roll with visual fixation on an axial target, the rotation axes of the eyes do not coincide with the gaze directions, and this produces 'skewing' of the vertical gaze. This 'skewing' is small and it is determined by the oculomotor response to roll stimulation of the vertical semicircular canals.

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Table 1:

Rotation axis convergence and gaze convergence during sinusoidal rotation with fixation.

Subject	Rotation axis convergence°		Gaze convergence°	
	Near	Far	Near	Far
BG	9.4	4.3	6.9	1.7
CG	11.6	6.7	6.9	1.7
KH	12.5	6.3	8.1	1.7
MA	30.6	18.6	8.0	0.8
MF	9.3	3.4	7.0	1.6
TO	6.8	2.1	8.0	1.5

Appendix

During sinusoidal roll oscillation, the torsional and vertical components of the slow phase vestibular response were not always related by a simple linear correlation. For some subjects, under some conditions (particularly with near fixation), plots of torsional angular velocity versus vertical angular velocity were slightly curved, rather than straight.

Further investigation of the angular velocity traces suggested that the binocular vertical angular velocities comprised both conjugate elements and disconjugate elements, which had identical profiles but opposite directions (signs). These symmetrical, disconjugate elements will be referred to as *converse* elements.

The vertical angular velocity for each eye could be expressed as a combination of conjugate and converse elements; where the conjugate part was given by the mean vertical velocity ($W_{y_mean} = (W_{yR} + W_{yL}) / 2$), and the converse part was given by the difference of vertical velocities of the two eyes ($W_{y_diff} = (W_{yR} - W_{yL}) / 2$) (Fig. 11A).

Hence, vertical angular velocity components,

for the right eye: $W_{yR} = W_{y_mean} + W_{y_diff}$

and the left eye: $W_{yL} = W_{y_mean} - W_{y_diff}$

The converse vertical velocities were closely synchronized to the temporal profiles of the torsional velocity components, and when combined with the torsional velocity components, produced the convergent eye rotation axes. Plots of torsional versus converse vertical velocity components were linear for all subjects. Regression lines through these plots gave values for the rotation axis convergence which were always within 5% of the original values, found by regressing the torsional velocity against the total vertical velocity component (Fig. 11B).

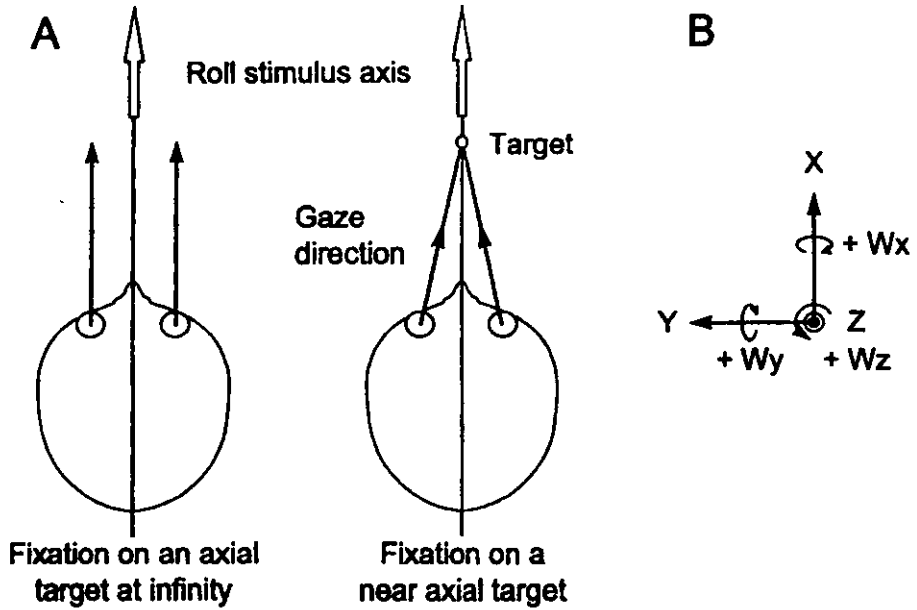


Figure 1. Top Views. A: The axis of rotation of the head during roll; and the gaze directions of the eyes, when the subject is looking straight ahead, or fixating on a near target. B: Head-fixed co-ordinate system, showing directions for positive torsional (W_x), vertical (W_y) and horizontal (W_z) angular velocities.

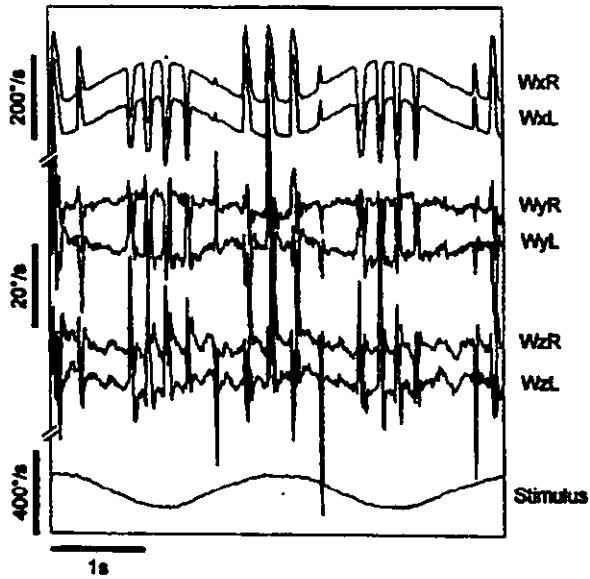


Figure 2. Torsional (W_x), vertical (W_y) and horizontal (W_z) components of the angular velocity of the right (R) and left (L) eyes, during sinusoidal oscillation with far fixation (Subject BG).

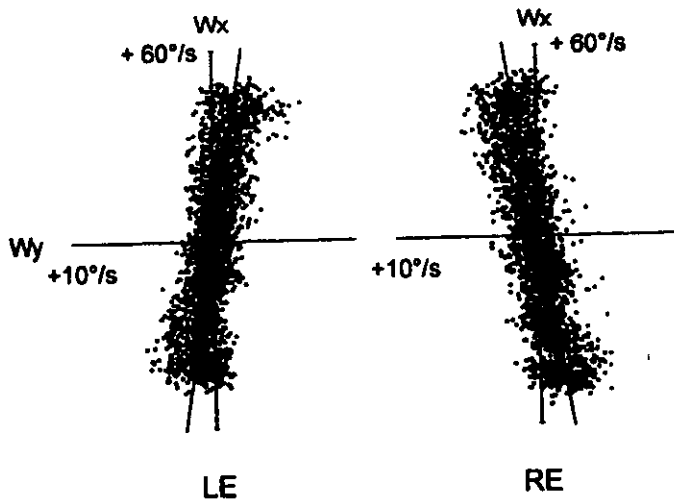


Figure 3. Plots of torsional (W_x) against vertical (W_y) components of the slow phase angular velocity of the right (RE) and left (LE) eyes, during sinusoidal oscillation with far fixation. Overlaid regression lines show the net eye rotation axes (Subject BG).

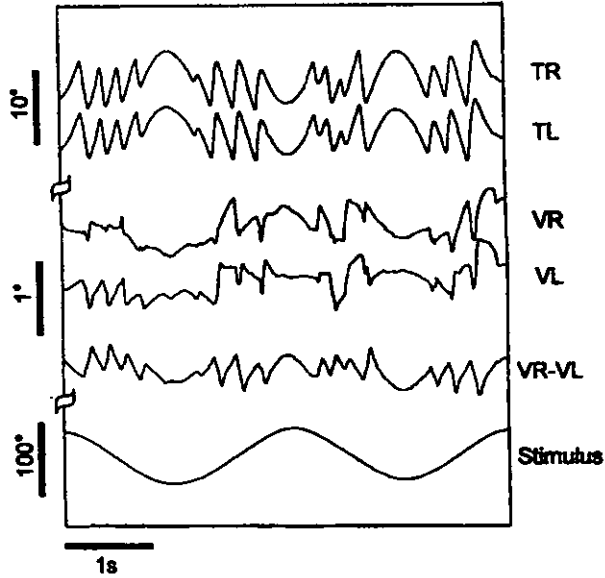


Figure 4. Torsional (T) and vertical (V) positions, of the right (R) and left (L) eyes, in Fick co-ordinates, during sinusoidal oscillation with far fixation (Subject BG). The VR-VL trace shows the vertical disconjugacy of the eyes.

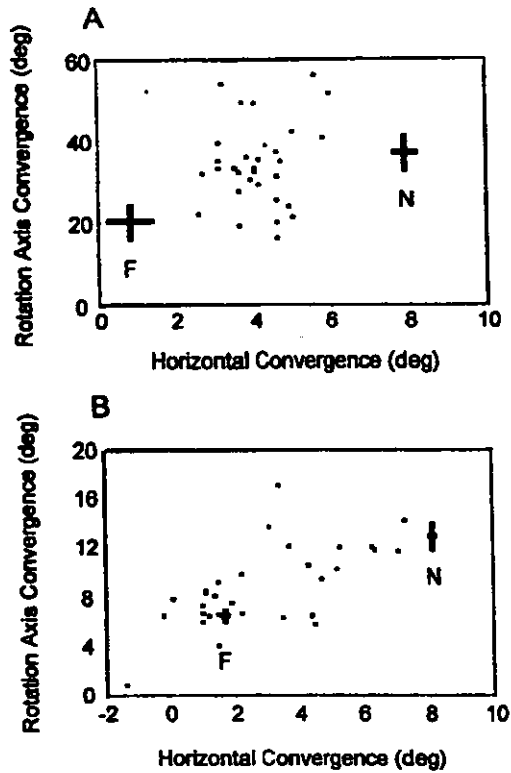


Figure 5. Rotation axis convergence versus horizontal gaze convergence for subject MA (A) and subject KH (B). The convergence angles were measured for each half-cycle of oscillation. Data points represent oscillation in the dark; crosses represent means and standard deviations during oscillation with near (N) and far (F) fixation targets.

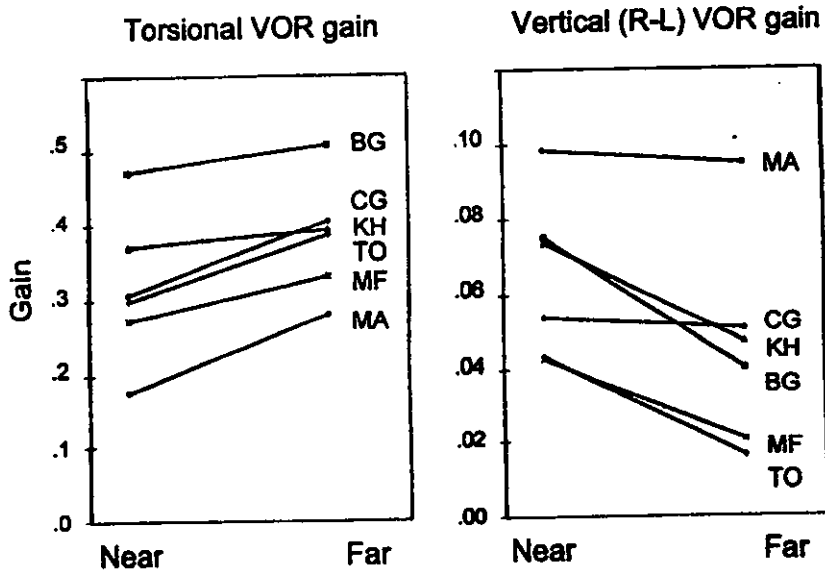


Figure 6. Velocity gains of the torsional and vertical (RE-LE) components of the slow phase response to sinusoidal oscillation, with near and far visual fixation, for all 6 subjects.

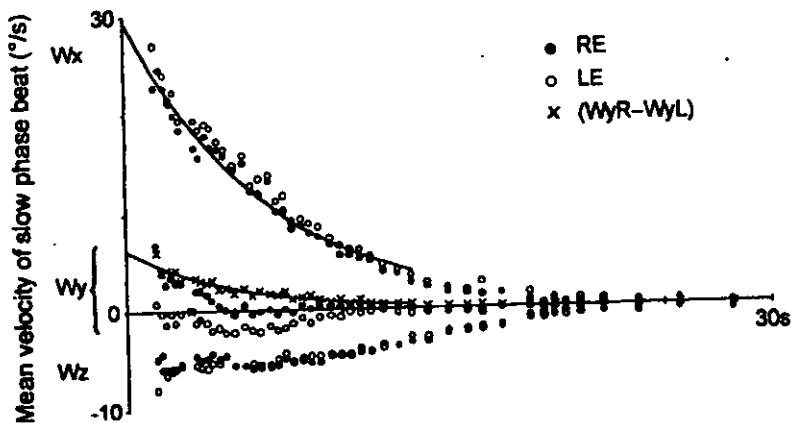


Figure 7. Stopping response (Subject CG), following constant velocity roll rotation to the right (top of head moving rightward). The mean torsional (W_x), vertical (W_y) and horizontal (W_z) angular velocities of each slow phase beat are plotted against the time from the deceleration of the stimulus. Exponential profiles were fitted to the torsional (W_x) and 'vertical vergence' (W_y) responses, to find the time constants.

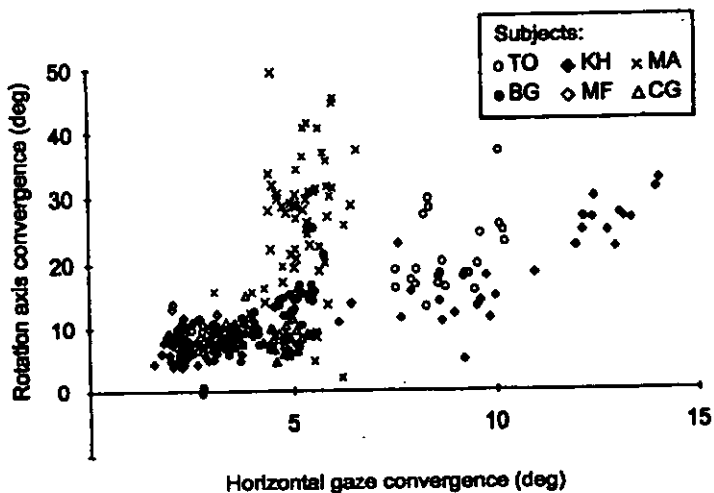


Figure 8. Rotation axis convergence versus horizontal gaze convergence for each slow phase of the stopping response nystagmus. For each subject, the data for stimuli in both directions have been pooled. One subject (MA) exhibited exceptionally large rotation axis convergence, which was consistent with his sinusoidal responses (Fig 5A).

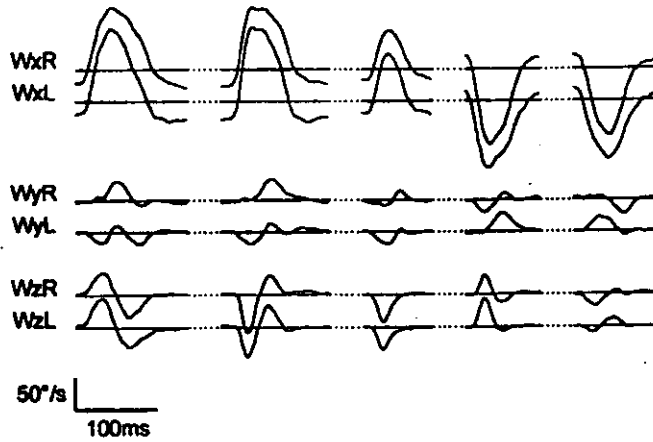


Figure 9. Examples of fast phase angular velocity profiles, of the right (R) and left (L) eyes, showing binocularly symmetrical torsional (Wx) and horizontal (Wz) traces, and asymmetrical vertical (Wy) components.

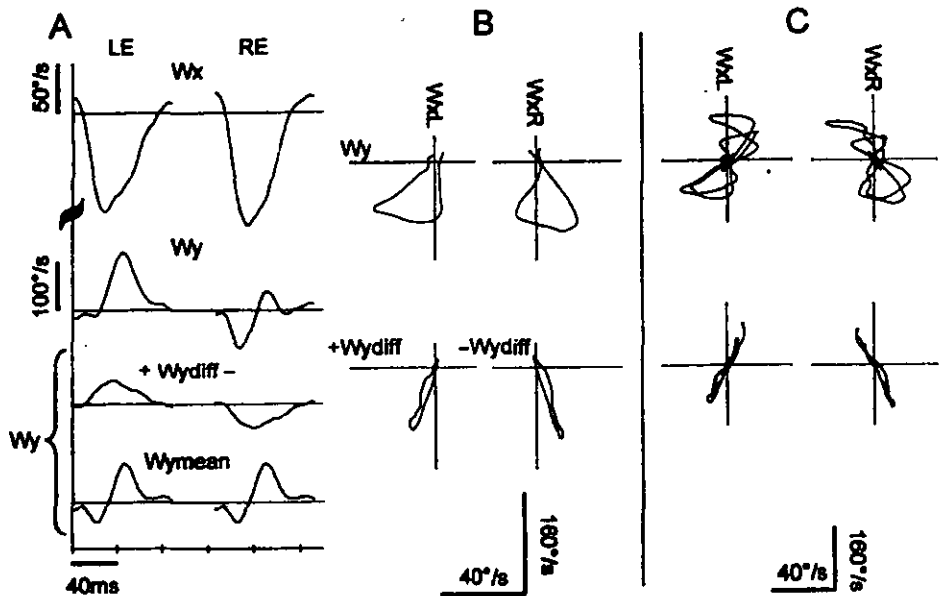


Figure 10. A: Torsional (W_x) and vertical (W_y) angular velocity profiles, of the right (RE) and left (LE) eyes, for a typical fast phase eye movement; together with the breakdown of the vertical velocity into converse ($\pm W_{ydiff}$) and conjugate (W_{ymean}) elements. N.B. Close synchronisation between converse vertical components and torsional angular velocities. **B:** Same fast phase as in A. Torsional angular velocity plotted against vertical angular velocity (upper), and against the converse vertical velocity component (lower). **C:** Angular velocity trajectories for 4 fast phases, showing the underlying, steady, convergent rotation axes predicted by combining the converse elements of the vertical velocity profiles with the torsional velocities.

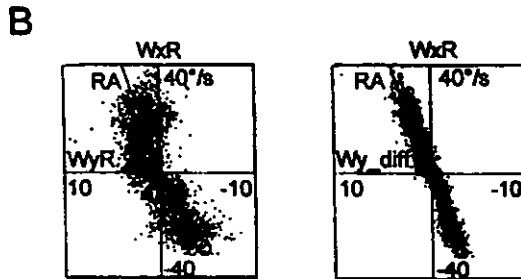
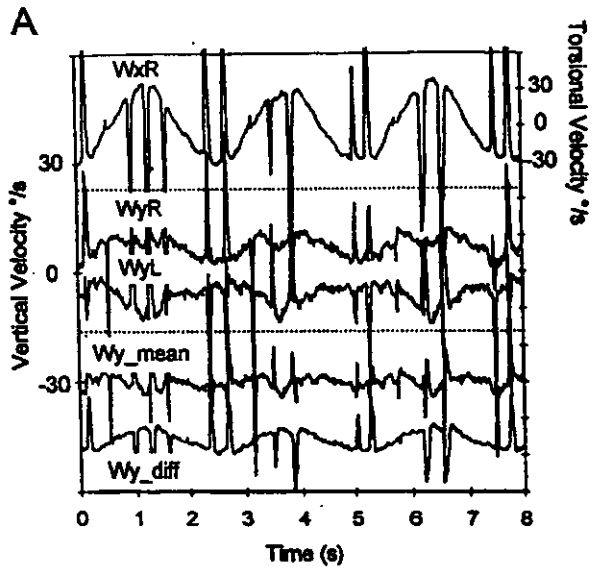


Figure 11. (Appendix). Angular velocity data for subject CG, with near fixation. A: Torsional (W_x) and vertical (W_y) velocity traces, along with conjugate (W_{y_mean}) and converse (W_{y_diff}) vertical velocity profiles. B: Slow phase data; regression plots to find the effective rotation axis (RA) of the right eye.

Ten rabbits (2.3–3.6 kg) were anaesthetized with halothane. The DPO was exposed aseptically and injected with 30–80 μ l of 20–30% HRP in phosphate-buffered saline (PBS, pH 7.4). The wound was sutured and antibiotics administered prophylactically. After recovery periods of 3–7 days the animals were deeply anaesthetized with halothane and perfused via the aorta with saline followed by PBS-buffered 1% paraformaldehyde and 1.5% glutaraldehyde. The brainstem was removed and transverse sections taken at 100 μ m. Sections were processed for peroxidase activity using diaminobenzidine as the chromogen (Mesulam, 1982). They were then mounted, air-dried and cover-slipped for microscopic examination and photography.

In all cases retrogradely labelled cells were found scattered in the rostral and dorso-lateral aspect of the NVmot. This is the region known to innervate the jaw-closing muscles (Matsuda *et al.* 1978). Such a trigonimotor innervation of the DPO suggests that this muscle is unlikely to be equivalent to the posterior belly of the digastric in other species. Our own dissections have failed to show any origin from the occipital bone. Its attachments to the maxilla and mandible imply an elevator function. Consequently, classification of this muscle as part of the digastric should be revised.

Supported by The Wellcome Trust (grant no. 046382/Z), University of Leicester and Nippon Dental University Foundation at Niigata.

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Visual stabilization during dynamic head roll in vestibular human subjects

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We have measured the effects of voluntary oscillating head roll (about an occipito-nasal axis) on ocular compensation and on the apparent movement of the visual world in three chronically vestibular subjects.

Movement of the eyes in the head was measured by video-oculography (Scheerer *et al.* 1991) with head roll amplitudes of 25–40 deg (peak to peak). Ocular counter-roll was a small fraction of the head movements, 3–8% at 0.33 Hz and –2% to 8% at 1 Hz, with few torsional saccades. This compares

with a gain of 40–70% between saccades in normals (Collewijn *et al.* 1985).

The patients were little impaired in setting a static subjective visual vertical (SVV) in the dark. Only one of the three set a consistent tilt (3.7 ± 0.2 deg, mean \pm s.e.m., $n = 3$) outside the 95% confidence limits (± 2.6 deg) based on eight normal subjects. The average s.d. for settings from random starting angles was 0.99 deg in the patients and 0.74 deg in normals. The effects of static 20–40 deg head tilt on SVV (Müller effect) were similar, with SVV having an actual tilt of $-12 \pm 11\%$ of head tilt in the patients (mean \pm s.e.m., $n = 3$) and $-11 \pm 4\%$ in normals ($n = 8$). In neither group was SVV significantly affected by a 10 N sideways force applied to a band around the head.

The effect of head roll on stability of the visual world was assessed with apparatus that measured the angle of head tilt and varied the tilt of a stimulus (a line of dots, viewed otherwise in the dark) in proportion to this angle (Gardner-Medwin *et al.* 1990). The subject adjusted the gain of this relationship until the line appeared stable. For the patients this gain was $24 \pm 10\%$ at 0.33 Hz and $32 \pm 15\%$ at 1 Hz (mean \pm s.e.m., $n = 3$) compared with normals: $8.0 \pm 2.1\%$ at 0.33 Hz and $7.0 \pm 2.0\%$ at 1 Hz ($n = 8$). Note that these gains are positive (opposite to the Müller effect). With oscillating roll, unlike static displacement, subjects generally (excepting one normal subject) required the stimulus to move in the same direction as head tilt to appear stable. This effect was larger in vestibular subjects, but less than the 92–102% gain required to stabilize the tilt of the retinal image, based on the measured counter-roll. The patients were less consistent in adjusting the gain for maximum stability: the mean s.d. for repeated settings was 20% for patients and 9% for normals. We conclude that perceptual instabilities during oscillating head roll are more sensitive to vestibular less than static measurements, but that vestibular subjects achieve substantial perceptual compensation in other ways.

Supported by the MRC. The study has ethical approval.

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Binocular response to roll-motion in man

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Six normal subjects participated in a study (approved by the local ethics committee) assessing the effect of visual

fixation on 3-D binocular responses to roll-motion. Subjects were exposed to whole-body rotation about an earth-vertical, naso-occipital axis, whilst supine with head and trunk firmly restrained.

Stimuli: (I) Oscillations at 0.4 Hz, 60 deg s⁻¹ (s.d. 4 deg s⁻¹) peak velocity, under three conditions: (a) fixation of an earth-fixed light-emitting diode (LED), 47 cm from the subject's nasion (near), in an otherwise dark room; (b) fixation of the LED at 206 cm (far); (c) total darkness. (II) Constant velocity rotations of 40 s duration, at 57 deg s⁻¹ (s.d. 3 deg s⁻¹), in darkness, clockwise and counter-clockwise, after which the 'stopping responses' were measured. Eye movements were recorded using search coil signals sampled at 500 Hz. Angular velocities were expressed in an orthogonal head-fixed co-ordinate system and gains were obtained from the regression of slow phase eye velocity vs. stimulus velocity.

Results: (I) *Sinusoidal stimuli.* The torsional component of the response was conjugate, with a mean gain of 0.31 (s.d. 0.09) for the near LED, 0.33 (s.d. 0.07) for the far LED and 0.37 (s.d. 0.10) in darkness. The vertical component was disconjugate (skewing): the extorting eye depressed whilst the intorting eye elevated. The skew was measured by subtracting left eye from right eye recordings. Mean skewing gains were 0.064 (s.d. 0.02) for the near LED, 0.045 (s.d. 0.02) for the far LED and 0.065 (s.d. 0.03) in darkness. (II) *Stopping responses.* The mean peak velocity of the torsional component was 22 deg s⁻¹ (s.d. 4.4 deg s⁻¹) (gain 0.39), the velocity decayed exponentially with a mean time constant of 4.5 s (s.d. 1.5 s); skewing was also present, with 4.4 deg s⁻¹ peak velocity (s.d. 1.9 deg s⁻¹) (gain 0.09) and exponential decline (mean time constant, 5.8 s; s.d. 1.9 s). For both stimuli, the vertical component of the fast phase reset the eyes from the slow phase by disconjugate movements, which were slower (23 deg s⁻¹, s.d. 10 deg s⁻¹) than those of the torsional component (75 deg s⁻¹, s.d. 20 deg s⁻¹).

The study confirms that dynamic vertical canal stimulation with constant otolith input induces skewing of the eyes. The skew could result from a stronger action of the vertical recti than the oblique eye muscles during the predominantly torsional response. However, horizontal convergence during roll could induce vertical displacement of images across the fovea, enhanced by the fovea's position towards the temporal field of the retina. Active skewing could be generated to prevent vertical diplopia associated with rotation of the eyes about the roll axis. The latter hypothesis is consistent with the enhancement of the skewing with visual fixation on the near target.

Evidence for segregation of timing and velocity storage in ocular pursuit

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Although humans cannot voluntarily generate smooth eye movements of more than about 5 deg s⁻¹, repeated presentation of a moving target at regular intervals allows build-up of an internal store of motor drive that can then be used to initiate anticipatory movements. To establish whether timing of the anticipatory response can be separated from the motor storage effect, we examined the ability to generate anticipatory movements when the time between presentations is randomized, but the time of target presentation is indicated by an audio cue. Subjects sat, with head fixed, 1.5 m from a semi-circular screen on which a horizontally moving target was projected. Eye movements were measured by infrared oculography. The target executed sequences of twelve identical, constant velocity ramps to the right. Velocity varied from 12.5 to 50 deg s⁻¹ in separate sequences. The target was visible for 400 ms with a randomized interval of 2.25–3.75 s between presentations. To assess the effect of orbital starting position, target presentation was timed to start on the midline (M-R), end on the midline (L-M) or straddle the midline (L-R). Two small targets placed on the midline, 3 deg above and below the moving target, served for fixation and were continuously present. Subjects were required to hold fixation on the midline until an audio cue was given and then to initiate eye movements in preparation for ensuing target appearance which, within each sequence, occurred at a fixed time after the audio cue. Cue times of 300, 600 and 1200 ms were examined. Four subjects participated with local ethics committee approval.

All subjects generated anticipatory smooth movements prior to target appearance that were synchronized with the audio cue, despite randomization of target onset. Anticipatory performance was assessed by measurement of eye velocity 100 ms after target appearance (V100), prior to the expected influence of visual feedback. Values were averaged for the final ten presentations of each sequence and, since ANOVA revealed no significant effect of cue time on V100, further analysis combined cue times. For all starting positions, V100 increased significantly ($P < 0.001$ by ANOVA) with target velocity. This velocity scaling is an indicator of the functional relevance of the anticipatory movement. There was no significant difference in V100 between the M-R and L-R conditions, mean V100 for the two starting positions reaching 17.8 deg s⁻¹ (s.d. = 7.9) for the 50 deg s⁻¹ stimulus. V100 for the L-M condition was significantly ($P < 0.01$) less (24%) than for other start positions, but still reached a significant proportion of peak velocity. The results provide a clear indication that timing and velocity storage can be independently controlled through

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CONCLUSIONES

1. En seres humanos sin evidencia de lesión vestibular, durante los movimientos en el plano frontal, el estímulo dinámico de los canales semicirculares verticales, con aferencia otolítica estable, puede inducir movimientos oculares verticales disconjugados.
2. Durante la rotación en el plano frontal, el grado de vergencia ocular horizontal puede modular la respuesta vestibulo-oculomotora a este movimiento. Cuando aumenta la convergencia, la ganancia de velocidad del componente vertical aumenta, mientras la ganancia del componente de torsión disminuye.
3. Después de la rotación continua de la cabeza y el cuerpo en el plano frontal, las características temporales de la respuesta vestibulo-oculomotora parecen estar determinadas por las características mecánicas de los canales semicirculares.
4. En seres humanos sin evidencia de enfermedad neurológica, cuando se ejecuta una fase rápida en la que el componente principal es el de torsión, el componente vertical puede ser disconjugado.

El hallazgo reciente de divergencia vertical de los ojos, registrada mediante video-oculografía (Jáuregui-Renaud 1996), como parte de la respuesta oculomotora a un estímulo dinámico a los canales semicirculares verticales, requería ser confirmado mediante técnicas que permitieran descartar la presencia de posibles artefactos durante el registro oculomotor. La video-oculografía cuenta con los inconvenientes de un posible desplazamiento de las cámaras durante el movimiento, una frecuencia baja de muestreo y el de registrar bidimensionalmente

(video) un fenómeno tridimensional (movimientos oculares). Desventajas que no se tienen con el uso de la técnica de localización magnética. Sin embargo, durante la etapa I fue necesario utilizar la video-oculografía por motivos técnicos y sus implicaciones en la factibilidad del estudio. La segunda etapa se efectuó con la técnica de localización magnética. El hallazgo de la divergencia vertical de los ojos se confirmó con ambas técnicas de registro.

En la obscuridad los ojos de un ser humano normal pueden encontrarse en posiciones variadas, lo que facilitaría la presencia de movimientos oculares disociados. Los resultados mostraron que, durante movimientos en rol, la divergencia vertical de los ojos está presente con y sin fijación visual.

El estudio de las respuestas peri-rotatorias implica la posible presencia de artefactos relacionados con el movimiento, situación que se evita durante los registros post-rotatorios porque se realizan en condiciones estáticas. El proyecto de investigación incluyó el estudio de la respuesta vestibulo-oculomotora a rotaciones sinusoidales y después de rotación a velocidad continua. La divergencia vertical de los ojos se identificó durante ambos tipos de registro, peri-rotatorio y post-rotatorio.

El estímulo dinámico de los canales semicirculares verticales, sin variación de la información para los otolitos, resultó en disociación vertical de los movimientos oculares. Las proyecciones principales de los canales semicirculares verticales a los músculos extra-oculares producen acción de los músculos rectos verticales y oblicuos. En el hombre, la combinación de las acciones de estos músculos fue capaz de producir torsión conjugada asociada a un componente vertical disconjugado, en el que la intorsión se acompañó de elevación y la extorsión de depresión. Lo que sugiere que durante la contracción de estos músculos para

efectuar la fase lenta de la respuesta a rotaciones en rol, los rectos verticales actúan con mayor fuerza que los oblicuos. La persistencia de esta asociación entre los componentes de torsión y vertical cuando aumenta la convergencia ocular horizontal, sugiere que es la inervación muscular más que sólo un fenómeno mecánico lo que determina la disociación vertical de los ojos.

La dirección de los ejes de rotación de los ojos fue convergente y cambio en relación a la convergencia horizontal. El eje de rotación de cada ojo no estuvo alineado con el eje de rotación de la cabeza (estímulo), y durante la fijación visual su convergencia fue mayor de lo esperado por la posición del punto de fijación. Lo que es congruente con el hecho de que, en el ser humano, la posición ocular para una ganancia de torsión mínima (o posición primaria) es en exo- desviación (Bruno 1997).

Los hallazgos del estudio, aunados a que los sujetos negaron haber experimentado diplopia durante la rotación (con y sin instrumentos de registro), son congruentes con la propuesta de que, durante la contra-rotación ocular a las aceleraciones angulares de la cabeza en el plano frontal, la divergencia vertical de los ojos podría ser útil para evitar una posible diplopia durante la torsión conjugada de los ojos, debido a que la posición de la fovea es excentrica, hacia el campo temporal de la retina. Sin embargo, esta hipótesis deberá ser sometida a comprobación.

La evidencia de que las fases rápidas del nistagmus evocado, durante movimientos en rol, presenten componentes de velocidad complejos, con asimetría en el plano vertical, podría ser explicado por la acción antagonista de los pares de músculos que son necesarios para efectuar un movimiento rápido cuyo componente principal es el de torsión.

La confirmación y estudio de la respuesta binocular a los movimientos en rol, amplía los conocimientos sobre la fisiología de la respuesta vestibulo-oculomotora humana. Información que además es útil para comprender mejor la posible patogenia de la divergencia ocular vertical que se observa en pacientes con lesiones del tallo cerebral. Los resultados sugieren que no solo las alteraciones de la vía otolítica sino también las que afectan la vía de los canales semicirculares verticales podrían dar origen a movimientos oculares con disociación del componente vertical, cuando éste es dinámico.

APENDICE

Consideraciones Anatómicas y Fisiológicas

La organización del reflejo vestibulo-ocular depende principalmente de:

- 1) la orientación de los receptores vestibulares,
- 2) la posición y las características cinemáticas de los músculos extra-oculares y
- 3) las conexiones neuronales entre los receptores del laberinto posterior y los músculos extra-oculares.

Receptores vestibulares .

En cada laberinto óseo de los huesos temporales se encuentra contenido un laberinto membranoso, rodeado por líquido perilinfático. En la parte vestibular del laberinto membranoso se identifican dos tipos de receptores inmersos en endolinfa: las crestas ampulares de los canales semicirculares, que detectan rotación de la cabeza, y las máculas del utrículo y del saculo con sus membranas otolíticas, que detectan posición de la cabeza y su aceleración lineal.

Cualquier aceleración de la cabeza ocasiona un patrón único de activación de los receptores vestibulares. Las características de este patrón se encuentran determinadas por la orientación de los canales semicirculares y de las máculas y su relación al plano de la aceleración. En el ser humano, uno de los canales semicirculares está aproximadamente a 25° del plano axial (el canal horizontal), mientras que los otros dos canales se encuentran aproximadamente a 49° (el anterior) y 40° (el posterior) con respecto al plano frontal (Blanks 1975), de manera que el canal anterior derecho es casi paralelo al canal posterior izquierdo y *viceversa*. La superficie de la mácula utricular está orientada aproximadamente en el plano del canal semicircular horizontal; la mácula del saculo está en el plano sagital, formando un ángulo casi recto con la mácula utricular (Baloh 1990).

Las crestas y las máculas poseen células ciliadas especializadas para transformar fuerzas de fricción en impulsos neurales, cada célula posee numerosos cilios y un cinocilio. La deflexión de los cilios hacia el cinocilio produce despolarización mientras que la deflexión en sentido opuesto produce

hiperpolarización. En las crestas de los canales semicirculares verticales los cinocilios están orientados hacia los canales y en las crestas de los canales horizontales los cinocilios están orientados hacia el utrículo. Cada mácula otolítica se encuentra dividida por una zona central llamada estriola, a cada lado de la estriola los cinocilios de las células ciliadas se encuentran orientados en dirección opuesta (Baloh 1990) (Figura 1).

Las fibras del nervio vestibular tienen actividad espontánea, lo que hace posible que ocurran cambios bidireccionales en su frecuencia de descarga, de acuerdo con la deflexión de los cilios de las células ciliadas. El nervio vestibular está constituido por fibras de neuronas bipolares localizadas en el conducto auditivo interno. Estas neuronas hacen sinapsis en 4 núcleos vestibulares principales (superior, inferior, medial y lateral) y los núcleos vestibulares menores, así como con la porción vestibular del cerebelo (Gacek 1982).

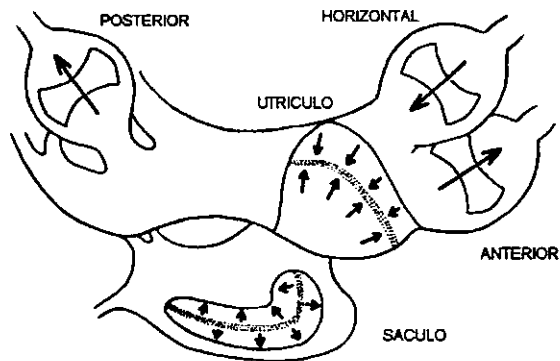


Figura 1. Vista lateral esquemática de los receptores del aparato vestibular de un oído derecho, donde se muestra la orientación de los cinocilios de los canales semicirculares (horizontal, anterior y posterior) y de las máculas otolíticas (utrículo y saculo) (Gacek 1982).

Músculos Extra-oculares

El ser humano tiene tres pares de músculos extra-oculares en cada órbita: un par de músculos rectos horizontales, un par de músculos rectos verticales y un par de músculos oblicuos. Los cuatro músculos rectos se insertan en el vértice de la órbita y en la esclerótica, en el hemisferio anterior del globo ocular. El músculo oblicuo mayor (o superior) se inserta en el vértice de la órbita, tiene una flexión en el borde orbitario donde atraviesa una polea y su segunda inserción está en la parte supero-externa de la esclerótica, en el hemisferio posterior del ojo. El músculo oblicuo menor (o inferior) se inserta en el borde externo del orificio superior del conducto nasal y en la esclerótica, en el hemisferio posterior del ojo (Testut 1983). La acción de los músculos extra-oculares se describe en la Tabla 1. El músculo recto superior actúa como elevador puro solamente cuando el ojo se encuentra en abducción de 23° (con respecto al eje X, fijo a la cabeza), la adducción del ojo hace que el músculo produzca intorsión además de elevación. El músculo oblicuo mayor sería un depresor puro sólo si el ojo pudiera estar en adducción de 51°, la abducción del ojo hace que el músculo produzca intorsión más que depresión (Leigh 1983).

Los músculos rectos superior, inferior y medial así como el músculo oblicuo menor están inervados por el nervio motor ocular común (nervio craneal III), el músculo oblicuo mayor se encuentra inervado por el nervio troclear (nervio craneal IV) y el recto lateral por el nervio abducens (nervio craneal VI). Los núcleos de los nervios oculo-motores están localizados en el tallo cerebral, cerca de la línea media, anteriores al cuarto ventrículo y al acueducto de Silvio.

Tabla 1. Acción de los músculos extra-oculares cuando los ojos están en posición primaria de la mirada.

Músculo	Acción Primaria	Acción Secundaria	Acción Terciaria
Recto medial	adducción	-	-
Recto lateral	abducción	-	-
Recto superior	elevación	intorsión	adducción
Recto inferior	depresión	extorsión	adducción
Oblicuo mayor	intorsión	depresión	abducción
Oblicuo menor	extorsión	elevación	abducción

Reflejo vestibulo-ocular

Las neuronas vestibulo-oculares de segundo orden están localizadas en los núcleos vestibulares superior medial y lateral, en el núcleo "Y" y aún en neuronas vestibulares primarias relacionadas al utrículo. Su vía de proyección principal es el fascículo longitudinal medio, otras vías son la formación reticulada, el tracto ascendente de Deiters y una vía que sigue una trayectoria cercana al *brachium conjunctivum* (Gacek 1982). Cada canal semicircular tiene influencia directa en la activación de un par de músculos extra-oculares. Para cada uno de estos pares de músculos, un músculo recibe inervación cruzada y el otro inervación no cruzada. Las principales conexiones entre los canales semicirculares y los músculos extra-oculares se describen en la Tabla II (Simpson 1985). Con respecto a las máculas otolíticas, estudios en animales han revelado que zonas específicas de cada mácula están asociadas a la activación de diferentes músculos extra-oculares (Fluur 1970a,b)

Durante rotación constante en el plano axial, las neuronas de los núcleos vestibulares presentan un incremento inicial del índice de descarga que después disminuye exponencialmente con una constante de tiempo igual a la de la respuesta oculomotora, pero mayor a la constante de tiempo de la cúpula de los canales semicirculares. Un mecanismo que 'memoriza' la actividad relacionada a la velocidad de fase lenta del ojo desempeña un papel importante en la producción del nistagmus vestibular, además del nistagmus optocinético y de las interacciones vestibulo-visuales. Durante el nistagmus inducido por estimulación vestibular, la actividad memorizada prolonga la duración de los movimientos oculares compensatorios (Cohen 1981).

Tabla II. Conexiones principales entre los canales semicirculares y los músculos extra-oculares.

Canal semicircular	Músculos ipsilaterales		Músculos contralaterales	
	excitación	inhibición	excitación	inhibición
Horizontal	Recto medial	Recto lateral	Recto lateral	Recto medial
Anterior	Recto superior	Recto inferior	Oblicuo inferior	Oblicuo mayor
Posterior	Oblicuo mayor	Oblicuo menor	Recto inferior	Recto superior

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