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Pathomechanism of mammalian downbeat nystagmus due to cerebellar lesion: a simple hypothesis

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Abstract

Most of the various hypotheses on the pathomechanism of the slight ocular upward drift in normal mammals and on the prominent downbeat nystagmus following cerebellar lesions assume an inherent vertical asymmetry in the central vestibulo–ocular pathways. In this paper we propose that this vertical asymmetry is simply based on the anatomical orientation of the six semicircular canals in the head which is right–left symmetrical but lacks symmetry in the cranio–caudal direction. Presuming that each semicircular canal elicits eye movements in a direction roughly in its anatomical plane, vectorial addition of the tonic resting activity of all six canals leads to a cancellation of horizontal and torsional eye movement components but leaves an important vertical (slow phase) upward component. This peripheral vestibular bias is centrally cancelled by floccular and paraflocculär inhibitory pathways which are related to the smooth pursuit system, but becomes disinhibited in the presence of posterior cerebellar lesions.

Keywords: Semicircular canals; Flocculus; Paraflocculus; Ocular rotation vectors; Alexander's law

Downbeat nystagmus (DBN) is a common ocular motor sign in patients with posterior cerebellar lesions close to the midline, especially if the flocculus and paraflocculus are involved [16]. Typically DBN shows an increase of upward drift (slow phase) velocity as patients look downward or laterally; with upward gaze, drift velocity decreases. In patients with DBN, the smooth pursuit system is usually impaired. A slight DBN may also be seen in some normal humans when attempting to fixate on an imaginary target in darkness [10]. In normal cats, DBN emerges when the animals are positioned in darkness in a position other than the normal prone position [14]; in normal monkeys, a DBN may be seen in darkness even in an upright position ([2] p. 1228).

The gain of the vertical vestibulo–ocular reflex (VVOR) seems to be symmetrical for upward and downward stimulation both in humans [1,4,6] and monkeys [9,12], but there is a striking asymmetry in the vertical velocity storage: Monkeys show longer time constants for downbeating than for upbeating vestibular nystagmus elicited by velocity steps about an earth vertical axis with the animals in a side position [12]. In humans, optokinetic afternystagmus (OKAN), which is directly related to the velocity-storage mechanism, is much stronger after upward stimulation, inducing downbeating optokinetic nystagmus (OKN) and OKAN [8]. Moreover, humans suppress downbeating vestibular nystagmus elicited by low-frequency (0.05 Hz) rotation about an earth vertical axis much less than upbeating nystagmus [5].

The exact pathomechanism of DBN is not yet known. Presently several explanations for the slight upward ocular drift in normal human and other mammals and for the prominent DBN in subjects with infratentorial lesions are put forward. Upward drift might be a result of

1. complex interactions between gravity-dependent forces acting on the eye bulb and of neuronal mechanisms, some of which depend on otolith information [10]
2. processing of otolith (saccular) signals by the central estimator of angular velocity [14]
3. central inhibitory connections exclusively onto the ante-

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rior semicircular canal pathways – lesion of these connections results in upward drift [11]
4. an imbalance in the central vertical vestibulo–ocular pathways [3]
5. an imbalance in the central vertical smooth pursuit tone [16].

Here we will propose a simpler hypothesis, which explains most of the main features of DBN. Our hypothesis is based on the orientation on the semicircular canals in the head as measured by Blanks et al. [7], and on the assumption that each of the semicircular canal elicits eye movements approximately in the direction of its anatomical plane [15]. The orientation of the semicircular canals and the direction of eye movements will be indicated relative to Reid coordinates (stereotaxic horizontal = plane trough orifices of the outer ear canal and lower rims of the orbitae). The 3D orientation of each SCC will be characterised by the normal on the respective anatomical canal plane. This vector is named the 'sensitivity' vector, as it is oriented parallel to the axis, about which angular rotation elicits the strongest response in the corresponding canal afferents. Compensatory eye movements elicited by rotation about an axis parallel to the sensitivity vector and by excitation of the corresponding canal afferents are considered to have an angular rotation axis parallel to the sensitivity vector but with opposite polarity (Fig. 1A). Eye movements will be expressed as angular eye velocity vectors, which are oriented parallel to the instantaneous angular rotation axis; their length corresponds to the velocity of the eye about this axis. x, y and z denote the occipito–nasal, interaural, and caudo–cranial axes of the Cartesian coordinate system, respectively. Thus, roll (x-axis), pitch (y-axis), and yaw (z-axis) movements of the head induce torsional, vertical, and horizontal eye movements, respectively.

Fig. 1B illustrates the projection of the corresponding

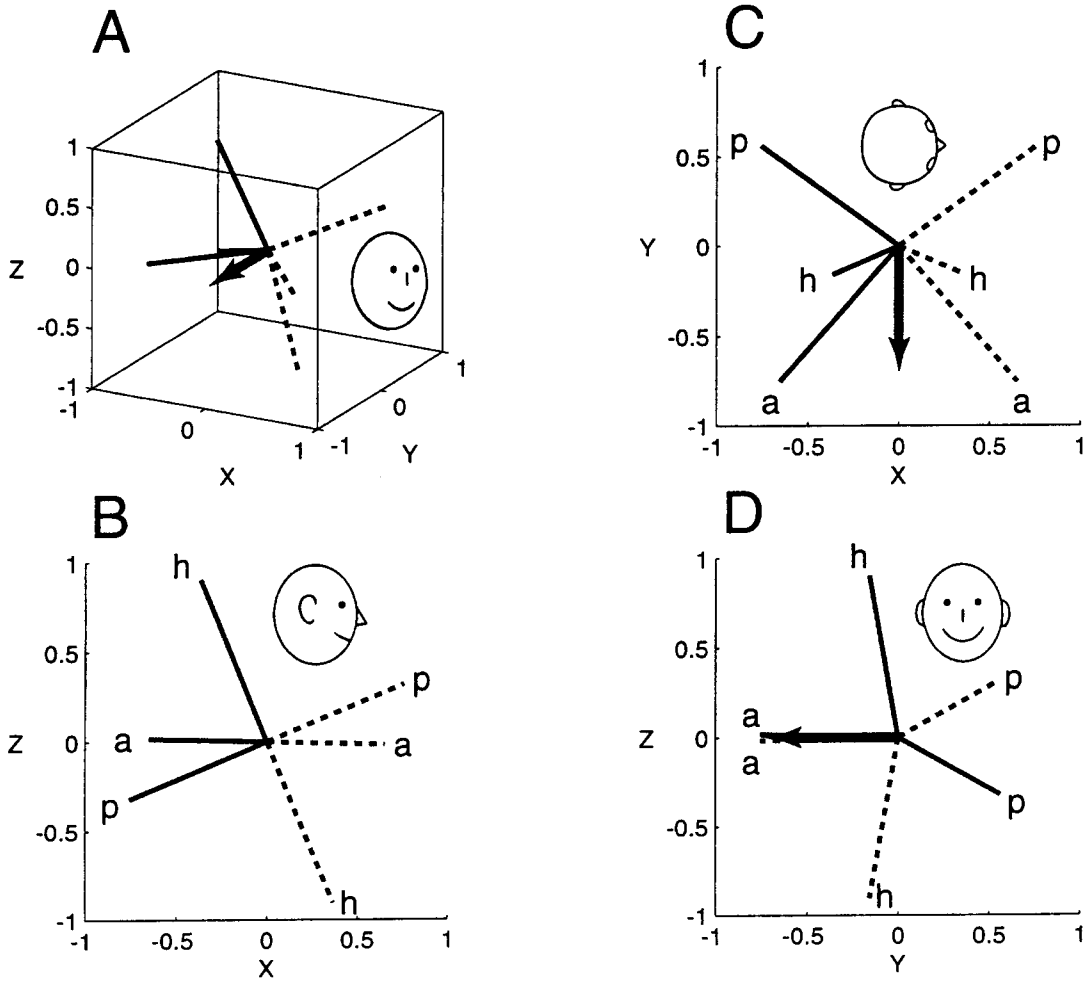

Fig. 1. Angular eye velocity vectors of human semicircular canals relative to Reid stereotaxic coordinates (according to data from Blanks et al., 1975 [11]). h, horizontal canal; a, anterior canal; *P*, posterior canal. (A) Three-dimensional reconstruction; broken lines and full lines illustrate right and left semicircular canal vectors, respectively; signs of direction according to the right-hand rule. (B) Projection on sagittal plane; note that each canal vector of the right side has exactly the opposite direction of its contralateral counterpart, vectorial addition of all canal vectors thus results in a zero vector in this plane. (C) Projection on the horizontal plane, note the right–left symmetry about the x-axis, but the missing symmetry about the y-axis, vectorial addition of all canal vectors therefore results in a negative y-vector. (D) Projection on the frontal plane; vectorial addition of all canal vectors results in a negative y vector. This corresponds to upward slow eye movements.

angular eye velocity vectors of the six semicircular canals onto the sagittal plane. The ocular response to angular acceleration stimuli is generated by vectorial addition of the responses elicited in each canal. The high resting discharge in the primary vestibular afferents may also induce such eye movements at rest, but due to the right–left symmetry of the head, vectorial addition will cancel these responses in the sagittal plane, i.e. the x and z components become zero (Fig. 1B). In vertebrates, however, there is no up–down symmetry of the semicircular canals, as it is for the whole body, and therefore the semicircular sensitivity vectors of both labyrinths do not necessarily nullify each other in their y components (vertical eye movement direction). In fact, Fig. 1C,D shows that both horizontal canals have a slightly negative y component, the posterior canals have a moderately positive y, while there is a stronger negative y in the anterior canals. The vectorial sum of the unit vectors of all semicircular canals on both sides yields a vector $(x, y, z) = (0.0, -0.7, 0.0)$. Presuming that stimulation of the afferents of a single semicircular canal produces eye movements roughly about an axis parallel to its sensitivity vector, the spontaneous resting discharge of all semicircular canals thus will generate a constant upward (negative y component) drift of the eyes. In normal subjects, this drift is probably counteracted by cerebellar inhibition of central vestibular pathways. This mechanism is probably tightly linked to the pursuit system, which minimises retinal slip by permanent calibration of the inhibition onto the negative vestibular y-bias. In the presence of floccular and paraflocculars lesions, the disinhibited negative y-bias becomes evident in a constant ocular upward drift. Owing to undisturbed brainstem ocular motor control systems, the upward eye drift is periodically reset by saccades, resulting in a downbeat nystagmus. The tight link between the pursuit system and this cerebellar inhibition is corroborated by the clinical experience that smooth pursuit eye movements are usually impaired in patients with DBN.

The gaze direction dependency of the intensity of DBN, i.e. an increase of upward drift (slow phase) velocity as patients look downward and a decrease with upward gaze, corresponds to Alexander's law described for pathological horizontal vestibular nystagmus. An active disabling of the velocity storage and the neuronal integrator in order to minimise the effects of the false input from the vestibular pathways has been proposed as the pathomechanism for this phenomenon [13]. Due to these reductions of vestibulo–ocular reflex time constants, gaze-evoked nystagmus occurs and is superimposed on the pathological direction-fixed spontaneous nystagmus, resulting in an increase in nystagmus when looking in the direction of the fast phase and in a decrease of nystagmus when looking in direction of the slow phase. In patients with DBN, there is not only an active reduction of the vestibulo–ocular reflex time constants but the underlying cerebellar lesion decreases the time constants already by itself.

Head-position (relative to gravity) dependent modulation of the DBN intensity [14] indicates some otolith influence upon its generation, but according to our hypothesis, the otolith input is only a modulatory, not the primary, drive of DBN.

In conclusion, there is no doubt that DBN is a sign of a central and not of a peripheral vestibular lesion. However, while the previous hypotheses on its pathomechanism presumed some inherent up–down asymmetries in the central pathways, we propose here that the mere anatomical orientation of the six semicircular canals results in an important asymmetry of the spontaneous input from the vestibular periphery. This asymmetry, however, occurs exclusively for the vertical direction, horizontal and torsional components are perfectly cancelled by vectorial addition of the signals from all canals. Normally, this tonic asymmetry is nearly perfectly suppressed by posterior-cerebellar central mechanism, but emerges uninhibited when these cerebellar structures are lesioned.

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