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Dissociation between canal- and otolith-function in cerebellar atrophy

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Sirs: Vestibulo-cerebellar degeneration affects the vestibulo-ocular reflex (VOR). For instance, the capacity to modify VOR gains (via the flocculus [1, 2]) or to suppress vestibular nystagmus by changing the head re gravity (via the nodulus [3, 4]) may be impaired. Cerebellar patients may even demonstrate bilateral vestibular loss [5]. Whether downbeat nystagmus (DBN), an ocular motor sign frequently found with vestibulo-cerebellar degeneration, results from asymmetric vertical VOR (VVOR) function, remains debated [6]. Alternatively, DBN may be caused by loss of vertical floccular Purkinje cells [7], asymmetries in vertical smooth pursuit pathways [8, 9], or dissociation of coordinate systems for vertical saccade generation and gaze-holding [10]. DBN is also influenced by otolith (OL) signals [11, 12].

We report on a patient (m, 82 yrs) with idiopathic late-onset cerebellar degeneration, in whom brain MRI demonstrated profound atrophy of the flocculus, whereas atrophy of nodulus and uvula was only mild (Fig. 1). Considering the relatively focal nature of the cerebellar degeneration, we asked whether semicircular canal (SCC)-related reflexes, which are mediated mainly by the flocculus, and OL-related reflexes, which are mediated primarily by the nodulus, are differentially affected in this patient. Since he exhibited prominent DBN, we also explored whether VVOR gains were asymmetric, i.e. lower during downward than during upward head rotations.

The patient gave informed written consent. The protocol was approved by the local ethics committee. *Vestibular-evoked potentials* (VEMPs) were registered from the sternocleidomastoid muscle on both sides [13]. The *caloric response* was assessed with electronystagmography (monoaural irrigation on either side, water temperatures 30 °C and 44 °C). Q*uantitative head impulse testing* was performed as described in [14]. S*tatic ocular counterroll* in sustained whole-body roll positions and *gravity-dependent modulation of DBN* along the pitch plain were tested on a three-axis motor-driven turntable [12].

Bilateral loss of SCC function was documented by absent caloric responses (not shown) and subtotal gain reductions of the VOR along the planes of all SCCs (Fig. 2A). Intact OL function was demonstrated by reproducible VEMP (threshold at 95 dB on both sides), preserved static ocular counterroll (Fig. 2B), and prominent modulation of DBN in the pitch plane with maximal slow-phase eye velocity in the prone position (Fig. 2C).

SCC- and OL-dependent reflexes are mediated by different parts of the vestibulo-cerebellum. The flocculus is important for the control of the angular VOR [1, 2], while the nodulus and uvula are mainly involved in the control of OL-related reflexes [3, 4]. In our patient, the dissociated vestibular deficits with impaired SCC-dependent, but preserved OL-dependent reflexes, might therefore be best explained by the pattern of the vestibulo-cerebellar degeneration predominantly affecting the floccu-

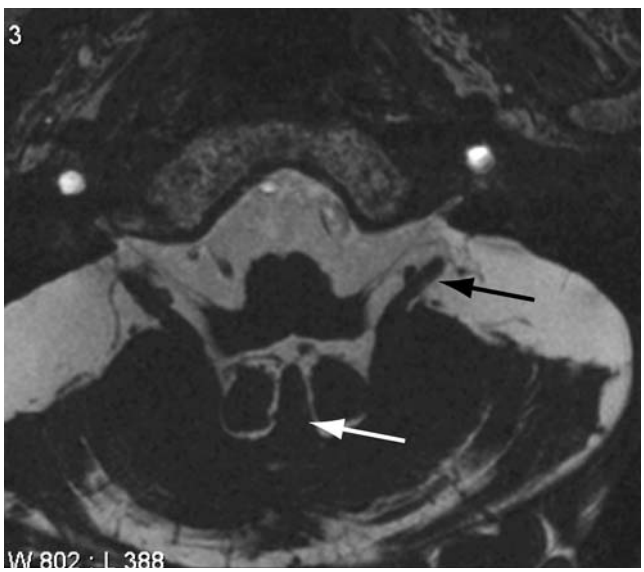

Fig. 1 High resolution MR with a Ciss sequence covering the cerebellum (slice thickness 0.85 mm) shows marked atrophy of the flocculus (black arrow) bilaterally, while the nodulus (white arrow) is relatively spared

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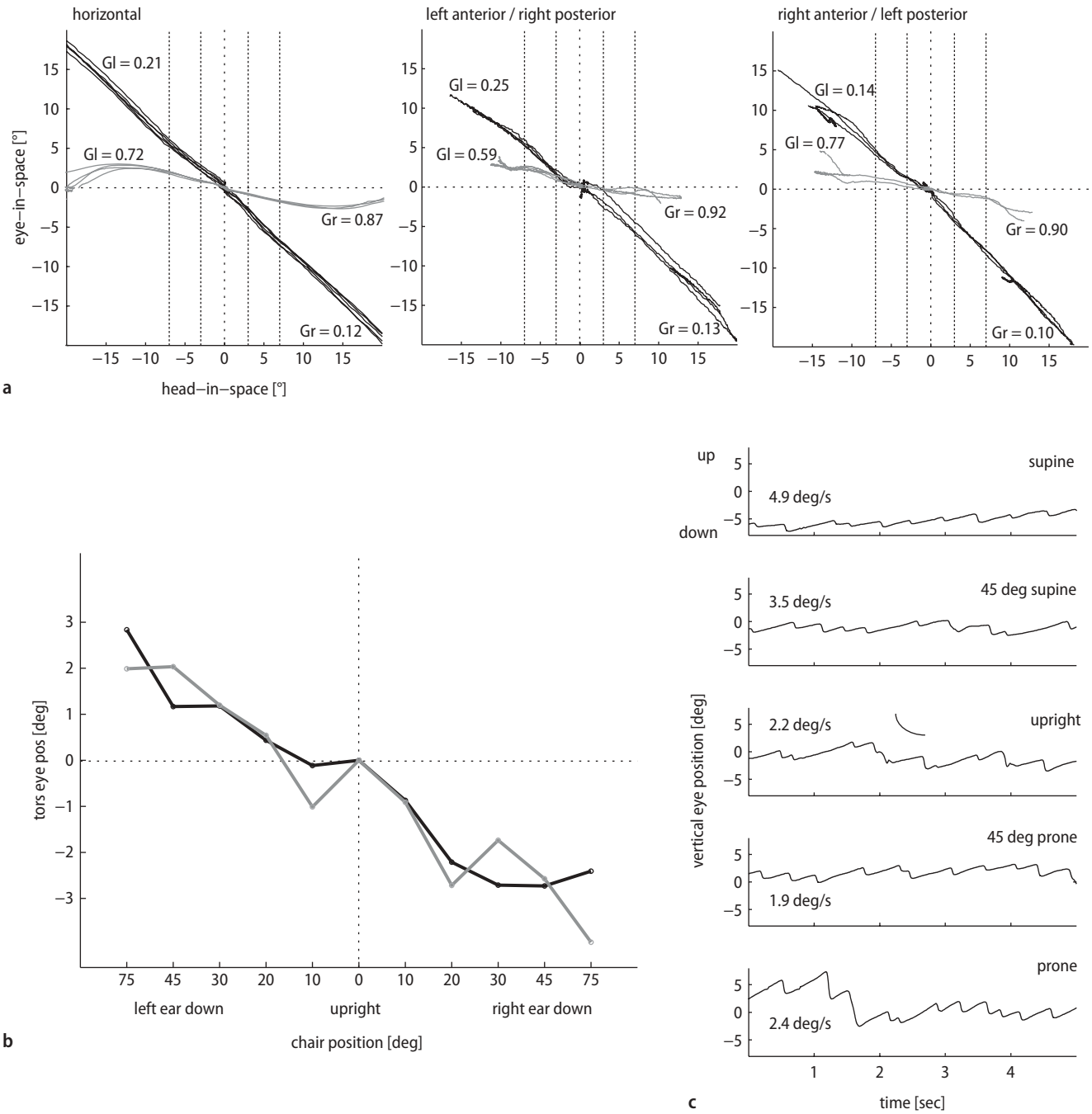

Fig. 2 Data are presented in coordinates used by clinicians, i.e. eye rotations to the right, up, and clockwise from the subject's point of view are positive. **A** Search-coil recordings of eye and head movements in space during head impulses in the directions of all six semicircular canals (SCC). *Left panel:* horizontal impulses to the right (positive) and to the left. *Middle panel:* vertical-torsional impulses in the plane of the right posterior (positive) and left anterior SCC. *Right panel:* vertical-torsional impulses in the plane of right anterior (positive) and left posterior SCC. *Black traces:* recordings in the patient; the vestibulo-ocular reflex (VOR) is markedly reduced in all directions. *Grey traces:* recordings in a healthy subject for comparison. *Gr, Gl:* VOR gains. **B** Static ocular counterroll testing on three-axis motor driven turntable (Acutronic, Jona, Switzerland): Modulation of torsional eye position in response to static whole-body roll tilt (75, 45, 30, 20, and 10° left- and right-ear-down) positions, while the subject was looking straight ahead at a laser dot. *Black traces:* recordings of the patient; the modulation of static ocular counterroll as a function of head roll was similar in right- and left-ear down positions. *Grey traces:* recordings in an age-matched healthy subject (f, 74 yrs old) for comparison. **C** Modulation of downbeat nystagmus slow-phase velocity as a function of whole-body position in the pitch plane. Representative sections of vertical eye position traces (duration 5 s) are shown for each of the five turntable positions. The patient directs his gaze towards a flashing laser dot straight ahead. The median vertical slow-phase eye velocity for each section is indicated. Upward ocular drift was maximal in prone and minimal in the supine position

lus, but relatively sparing the nodulus. Whether a primary degenerative process of both cerebellar and brainstem structures led to the subtotal loss of VOR function, remains unclear [5]. Alternatively, since the cerebellar network is particularly prone to retro- and transneuronal degeneration [15], the severe reduction of VOR gains in our patient with long-standing and marked floccular atrophy is probably caused by a mechanism of secondary retrograde degeneration of floccular brainstem target neurons involved in angular VOR gain control. Clearly, this hypothesis needs further confirmation by histopathological studies. A peripheral origin of the vestibular deficits cannot be ruled out, but seems unlikely, because – to our best knowledge – no peripheral vestibular disease would cause such selective and severe impairment of SCC function, while sparing the otolith pathways. Finally, the persistence of DBN despite massively decreased vertical SCC function in our patient speaks against the hypothesis that DBN in general results from a VVOR asymmetry [6], but rather supports the theory that some cases of DBN may be caused by loss of vertical gaze-velocity sensitive floccular Purkinje cells, which have predominantly downward on-directions [7].

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