Deviations of the subjective visual vertical in the roll or fronto-parallel plane occur commonly in disorders of the brainstem and have been extensively explored. In contrast, little is known about deviations in other directions. The present retrospective study focused on deviations in the pitch (sagittal) direction in 176 patients with a wide variety of disorders. The test task was to set a self-illuminated rod in the apparent upright position, in total darkness. Abnormal results (outside $\pm 4^\circ$) were recorded in 58% of the subjects. Negative (top backward) deviations were the most common, particularly with mass lesions in the pineal region, obstructive hydrocephalus, cerebellar lesions and crowding at the craniocervical junction. Positive and negative deviations were about equally common with focal intra-axial lesions. Negative deviations appeared related to dorsal locations of lesions and vice versa. Normal pressure hydrocephalus, Parkinson’s disease and progressive supranuclear palsy were associated with smaller deviations, without a clear directional preponderance, and a larger individual variability. Most subjects lacked overt clinical corollaries. The most common ocular signs were aqueduct syndromes ($n=17$) and ocular tilt reactions ($n=12$), which were associated with deviations in 47 and 92% of instances, respectively. Subjective corollaries of deviation were never reported, not even by those subjects who showed a dramatic improvement upon resolution of the underlying condition. Deviations were also assessed in roll in a subgroup of 40 patients with focal lesions. Thirty subjects returned abnormal results: 13% in roll, 47% in pitch and 40% in pitch and roll. The direction of roll deviation appeared primarily related to laterality, with clockwise deviations with right-sided lesions and vice versa. All subjects with ocular tilt reactions had combined pitch and roll deviations, implying a common neural substrate. Correlation analyses, geometrical modelling and experimental self-observations indicated that deviations in pitch were attributable to cyclotorsional asymmetries between the eyes. The frequent co-existence of abnormal pitch and roll results implies that the true axis of deviation in focal brainstem disorders commonly falls outside traditional reference planes. The term ‘visual upright in three dimensions’ is suggested to identify unrestricted measurements, preserving the established term ‘visual vertical’ for measurements confined to the roll plane. Assessment of the visual upright in three dimensions provides a new, quantitative angle on brainstem disorders. The test appears useful for identifying a ubiquitous yet clinically silent feature of brainstem disease and also for monitoring the evolution of underlying conditions. More detailed explorations appear well motivated.

**Keywords:** subjective visual vertical; brainstem disease; neurodegenerative disorders; balance disorders; stereo vision

**Abbreviation:** PSP = progressive supranuclear palsy
Introduction

Arranging objects like picture frames to the upright position is so easily done that errors are almost unheard of. Nevertheless, consistent deviations of the subjective visual vertical can easily be elicited in several disorders and more particularly those involving the brainstem and the vestibular system, by excluding environmental visual references to true upright (Friedmann, 1970). In the following, focus will be kept on central disorders, leaving disorders of the peripheral vestibular system aside. Deviations constitute by far the most common sign of acute brainstem damage. The largest study involved 111 patients, among whom 94% obtained abnormal test results (Dieterich and Brandt, 1993a). Deviations are also common with thalamic, cerebellar and hemispheric strokes (Dieterich and Brandt, 1993b; Brandt et al., 1994; Baier et al., 2008; Pérennou et al., 2008). Deviations have attracted particular interest in the context of ocular tilt reactions, i.e. the triad of skew deviation, ocular torsion and head tilt, and detailed pathophysiological models have been elaborated (Dieterich and Brandt, 1992; Brandt and Dieterich, 1995; Brodsky et al., 2006). Although most studies have been performed in laboratory settings, bedside evaluations can be done with a simple wastepaper basket provided with diameter markings on the inner and outer bottom surfaces; the basket body serves to exclude external cues (Frisén, 2000; Zwergal et al., 2009a).

A feature common to the cited studies is their exclusive focus on deviations in the roll or fronto-parallel plane. Little is known about deviations in other directions. Following up the clinical observation that subjects with hydrocephalus tend to have difficulties with balance in pitch or sagittal depth, Wikkelsø et al. (2003) examined the subjective visual vertical in pitch in patients with either obstructive hydrocephalus or primary normal pressure hydrocephalus, using a simple, self-illuminated rod that could be tilted in the sagittal plane. Results were inconclusive, without a clear preponderance of deviations in one or the other direction. However, one case of secondary normal pressure hydrocephalus presented a deviance of deviations in one or the other direction. Results were inconclusive, without a clear preference. In addition to the clinical neuroopthalmological examinations, patients were assessed neurologically by the referring physicians, usually on the neurological or neurosurgical services. All subjects were examined by CT, MRI or both. Deviations have been associated with a positive value with rightward tilts and vice versa, as seen from the subject’s side. An earlier version of the test device, which measured deviation in pitch only (Wikkelsø et al., 2003), was used in the initial phase of data collection, occasionally in combination with the wastepaper basket roll test (Frisén, 2000).

The results of all clinical, ancillary and neuroradiological examinations were retrieved and formed the basis for allotting subjects to selected study groups. For this first exploration, study groups were broadly categorized as described below.

Focal lesions

Focal lesions were defined by neuroimaging. The lesion’s approximate centre of gravity was assigned to the thalamus, midbrain, pons, medulla oblongata, cranio-cervical junction, cerebellum or pineal region. All patients assigned to the pineal region group had circumscribed mass lesions or cysts and normal cerebral ventricles. Patients with pineal masses and hydrocephalus were assigned to the obstructive hydrocephalus group defined below.

Diffuse lesions

Diffuse lesions were defined either by neuroimaging evidence of abnormally large cerebral ventricles, with or without aqueduct stenosis, or by clinical evidence of a neurodegenerative movement disorder. Patients were assigned to one of the following groups: (i) obstructive hydrocephalus; (ii) normal pressure hydrocephalus; (iii) Parkinson’s disease; or (iv) progressive supranuclear palsy (PSP). To facilitate overview, staging of severity of disease was omitted. Normal controls were recruited from staff and among patients’ partners.

Visual upright

The visual upright was tested with a 0.4 m long, self-illuminated acrylic rod supported on a tripod stand (Fig. 1). The rod mount allowed simultaneous tilting around pitch and roll axes. Each axis was provided with a slight resistance to movement to exclude gravity cues to true upright. Tilt angles were displayed electronically and could be read to the nearest 0.3°. Deviations in pitch were assigned a positive value when the rod’s upper end was tilted away from the subject and a negative value for the opposite direction. Deviations in roll were assigned a positive value with rightward tilts and vice versa, as seen from the subject’s side. An earlier version of the test device, which measured deviation in pitch only (Wikkelsø et al., 2003), was used in the initial phase of data collection, occasionally in combination with the wastepaper basket roll test (Frisén, 2000).

All subjects were tested binocularly. Any refractive errors were left uncorrected to ensure freedom from spectacle aberrations. Roll angles were also occasionally assessed monocularly with the rod’s pitch axis locked in true vertical.

The subject was comfortably seated in the upright position in a sturdy chair, without a head restraint, and with both feet firmly planted on the floor. The rod’s roll axis was positioned in the subject’s mid-sagittal plane, at eye level, with the rod centre at 0.4 m distance from...
Deviations in pitch

Thirty normal controls [mean (SD) age 45 ± 15 years] presented a mean deviation in pitch of −0.8° ± 2.4°, which was not significantly different from zero (P = 0.21). In the following, ±4° was considered normal. There were no significant correlations between age and individual means or standard deviations.

A total of 226 patients were examined for deviations in pitch. Six were excluded from analysis because of technical issues and 13 because of limited co-operation. Most of the latter had advanced Parkinson’s disease or PSP. Another 31 cases obtained final diagnoses other than those selected for study. Hence 176 patients were included in the analysis. Their mean (SD) age was 51 ± 20 years. All but eight were adults; 54% were males.

One hundred and two patients (58%) presented results outside normal limits; 68 (67%) of these had negative deviations. Because the direction of deviation may be meaningful on its own (see below), it is not appropriate to produce overall summary statistics. Instead, individual results have been grouped by diagnostic category for visual overview in Fig. 2A. Table 1 provides additional detail for the focal disorder group. As to variability within subjects, means and SDs were larger in the diffuse disorder group than in the focal one (3.0 ± 2.1 and 2.3 ± 1.2; P < 0.01) and both groups differed significantly from the normal group (1.6 ± 1.3, P < 0.01 and P = 0.02, respectively).

Turning first to the neurodegenerative movement disorder groups, Fig. 2A shows abnormal deviations in several cases within the Parkinson’s disease (n = 17) and PSP (n = 20) groups. However, the variation between subjects was large and cautions against the assignment of a typical direction of deviation. There was a somewhat clearer predominance of negative deviations among normal pressure hydrocephalus subjects, but the magnitudes were small (−2.1° ± 4.4°, n = 21) and may not be meaningful in the individual case. Five subjects with Binswanger disease, an important differential diagnosis to normal pressure hydrocephalus, obtained similar results (−4.9° ± 4.7°; P = 0.27). Because of their essentially multifocal disorders, these latter subjects were not included in the main study material.

The obstructive hydrocephalus and pineal groups presented preponderances of negative deviations (Fig. 2A), averaging −3.9° ± 5.1° (n = 45) and −3.9° ± 3.7° (n = 10), respectively. The obstructive hydrocephalus group contained a minority of subjects with positive deviations. Analysis of deviations in obstructive hydrocephalus subjects with aqueduct stenosis by level of stenosis did not reveal any clear associations.

The cranio-cervical junction (n = 11) and cerebellar groups (n = 12) evidenced predominantly negative deviations. There was one instance of a pronounced positive deviation in each group; the one in the cerebellar group had the largest deviation recorded in this material, 19.4° ± 1.6° (Fig. 2A). Because of the outliers, median values are more representative than mean values and equalled −5.7° and −5.2°, respectively.

The midbrain and pons groups were associated with large ranges of both positive and negative deviations, whereas the medulla group comprised predominantly positive deviations (Fig. 2A). The lack of clear relationships between direction of deviation and brainstem level shows that grouping by rostro-caudal level carries little information. Dorso-ventral segmentation may be more meaningful. Lacking natural segmentation landmarks, attention was directed to individual cases with small, intra-axial lesions. Unfortunately, such lesions were rarely encountered in the present study. However, four cases from the midbrain group, where positive and negative deviations were approximately equally common, indicated that negative deviations may predominate with dorsal lesions and vice versa (Fig. 3). Dorso-ventral sign associations could not be clearly demonstrated for the pons and medulla subgroups, where no instances
of focal ventral lesions were encountered. However, 10 out of the 11 cases with central or dorsal pontine lesions presented strongly negative deviations; the 11th case had a normal result. In the medulla group, there were four small lesions only, all of which were lateral infarcts associated with the Wallenberg syndrome; three had pronounced positive deviations and the one with the smallest lesion had a normal result.

A few subjects who had been taken ill acutely could be followed over time. Most showed a dramatic improvement within a few days and none had a deficit persisting over months (Fig. 4).

### Binocular versus monocular deviations in pitch

The results related above were obtained under binocular conditions. Monocular tests are also possible and raise the question of whether the outcomes of monocular and binocular measurements are related. Therefore, 13 subjects with a variety of lesions were tested under both conditions (Fig. 5). The correlation between right and left eye results proved to be strong (0.83, \( P = 0.003 \), Bonferroni correction), whereas the correlation between mean monocular and binocular results lacked statistical significance (\( P = 0.14 \)). Hence, results of monocular and binocular tests are not related and neither test can predict the outcome of the other. The different outcomes have important implications for attempts towards pathophysiological interpretations. A model can be proposed for the binocular situation but not for the monocular one.

### Binocular deviations in roll

Normal controls produced an average deviation of \(-0.2^\circ \pm 1.4\). In the following, \( \pm 3^\circ \) was considered normal. Roll measurements were available in a subgroup of 72 patients (Fig. 2B). Overall, deviations were smaller in roll than in pitch and the two measures did not correlate (Fig. 6A).

---

**Table 1** Pitch results with focal lesions subdivided by anatomical region and lesion type

<table>
<thead>
<tr>
<th>Region</th>
<th>Vascular</th>
<th>Mass</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thalamus</td>
<td>4–0–0</td>
<td>0–0–0</td>
<td>0–0–0</td>
</tr>
<tr>
<td>Midbrain</td>
<td>3–3–1</td>
<td>1–1–2</td>
<td>0–0–1</td>
</tr>
<tr>
<td>Pons</td>
<td>1–2–0</td>
<td>0–0–0</td>
<td>0–1–0</td>
</tr>
<tr>
<td>Medulla</td>
<td>0–0–0</td>
<td>1–1–0</td>
<td>0–0–0</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>0–0–0</td>
<td>1–1–0</td>
<td>0–0–0</td>
</tr>
<tr>
<td>Craniocervical</td>
<td>0–0–0</td>
<td>1–1–6 (AC(^b))</td>
<td>1–1–3</td>
</tr>
<tr>
<td>Pineal</td>
<td>0–0–0</td>
<td>0–4–6</td>
<td>0–0–0</td>
</tr>
</tbody>
</table>

\(^a\) Format: numbers of cases with positive deviations–no deviations–negative deviations.

\(^b\) AC = Arnold–Chiari types I + II.
Thirty-two cases belonged to the diffuse lesion group. The large majority had Parkinson’s disease or PSP and small deviations (0.3° ± 2.7° and 1.1° ± 1.6°, respectively). Only sporadic tests were made in the normal pressure hydrocephalus and obstructive hydrocephalus groups, all with normal results. Deviations in roll were more common and had larger amplitudes in the focal lesion group (n = 40, Fig. 2B), where 30 subjects returned abnormal results. Four of these (13%) returned abnormal results in roll only; these belonged to the midbrain, pons, medulla and cerebellar subgroups. Forty-seven per cent were abnormal in pitch only and 40% in both pitch and roll. Twelve patients with combined deviations had skew deviations and/or ocular tilt reactions of different severities; for simplicity they will be referred to as ocular tilt reactions. Plotting their deviations on roll and pitch axes revealed that individual observations could occupy any one of the four quadrants, with suggestive cross-wise relationships. Because of the limited number of observations, analysis benefits from removal of the direction signs. Collapsing all observations to one quadrant revealed a tight correlation (Fig. 6B). Incidentally, subjects with pronounced skew deviations are usually unable to perform binocular visual tests because of diplopia; there were six such instances among the patients who had to be excluded from testing. Those who were tested had recovered from their initial diplopia.

There were no clear relationships between directions of deviation in roll and rostro-caudal or dorso-ventral lesion levels. Analysis of cases with purely lateral intra-axial lesions (n = 12) indicated that positive deviations tended to be associated with right-sided lesions and vice versa. However, all three instances of the one-and-a-half syndrome (unilateral gaze paralysis plus internuclear ophthalmoplegia) presented normal results in roll but substantial deviations in pitch (−5.6°, −14.1° and −15.7°).

**Monocular deviations in roll**

Monocular results were available in 39 cases, all of whom had focal lesions. There was a frequent occurrence of asymmetry between the eyes (Fig. 7A). The regression coefficient is influenced by outlier observations and may not be meaningful by itself. The outliers themselves are reliable observations, however, and cannot be disregarded. Asymmetries in roll can be subdivided into two variants of disjugation: intorsions and extorsions. Intorsions are defined as clockwise rotation of the right eye around the line of sight and/or counter-clockwise rotation of the left eye (as seen from the examiner’s side). Similarly, extorsions are defined as counter-clockwise rotation on the right and/or clockwise rotation on the left. In a model to be elaborated in the ‘Discussion’ section, extorsions are expected to generate positive deviations in pitch and intorsions negative deviations. Intorsions and extorsions that are symmetrical with respect to the midline are very rarely encountered; the present material contained only one example of opposite directions (Table 2, Case 2). A rare occurrence is to be expected, as unilateral brainstem lesions principally will affect yoked pairs of oculo-rotatory eye muscles, causing roll in the same direction in the two eyes. The magnitudes are frequently dissimilar (Fig. 7A). Any interocular difference in roll defines intorsion or extorsion, depending on the sign.

The relationship between interocular differences in roll and deviations in pitch is best explored by attending to subjects with well-defined focal lesions (Table 2). Figure 7B shows that the
relationship is fairly well defined, with a correlation coefficient of 0.82 ($P < 0.01$).

**Combined deviations**

For an overview of combined measurements in roll and pitch, absolute values of deviations were collapsed over the study groups to two categories only, namely, diffuse and focal. Figure 8 shows that diffuse lesion results (open symbols) most often fell within normal limits and that abnormal results were more common in pitch than in roll. With focal lesions (closed symbols), abnormal results were more common overall and more common in pitch and combined pitch and roll than in roll only; deviations were generally larger in pitch than in roll.

**Discussion**

**Deviations in pitch**

There are few previous studies of deviations of the subjective visual vertical in pitch. The present report confirms the findings of Wikkelsø et al. (2003) of a large variability among patients with obstructive hydrocephalus and normal pressure hydrocephalus
but differs in the identification of a preponderant direction of deviation. Deviations have also been recorded in a small group of subjects with neglect caused by extensive right hemisphere strokes. These subjects also had deviations in roll and body tilts (Saj et al., 2005). Notably, deviations in roll have been described with lesions involving parieto-insular vestibular cortex lesions (Brandt et al., 1994).

In the present study, deviations in pitch were not confined to any specific group (Fig. 2A). The highest prevalences of negative deviations were encountered with obstructive hydrocephalus and lesions involving the pineal region, the cerebellum and the cranio-cervical junction. The highest prevalences of positive deviations were observed with posterior thalamic and medullary lesions, with the reservation that the number of observations was small. Both positive and negative deviations were recorded for most brainstem regions. These seemingly disparate outcomes probably reflect an anatomically widespread neural substrate for deviations in pitch.

Although a deviation in pitch by itself has a limited localizing value, the direction of the deviation might be expected to correlate with deficits of vertical gaze. The classical dorsal midbrain or aqueduct syndrome may be taken as an example. This syndrome typically debuts with convergence-retraction nystagmus on upward saccades and may progress to frank upgaze paralysis. Out of 17 instances observed here, eight presented normal results, five had positive deviations and four had negative deviations. Actually, the classical syndrome itself proved to have a limited localizing value, being encountered not only within the pineal, midbrain and obstructive hydrocephalus subgroups but also with thalamic and cerebellar lesions. Another condition associated with deficits of vertical gaze is PSP. Among the 20 cases studied here, 11 presented deviations outside normal limits but there was no predominant direction of deviation (Fig. 2A). Similar results were obtained for the 17 patients with Parkinson's disease. The PSP and the Parkinson’s disease groups presented unusually large within-subject variations, perhaps indicative of a cognitive

Table 2 Eye signs, deviations in pitch and roll (means ± SD) and torsion categories in well-defined focal lesions

<table>
<thead>
<tr>
<th>Case</th>
<th>Lesion</th>
<th>Eye signs</th>
<th>Pitch</th>
<th>Roll R + L</th>
<th>Roll R</th>
<th>Roll L</th>
<th>Roll R–L</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Fig. 3A</td>
<td>0</td>
<td>−2.5 ± 1.5</td>
<td>−4.0 ± 1.0</td>
<td>−3.9 ± 1.0</td>
<td>−2.7 ± 0.0</td>
<td>−1.2</td>
<td>Intorsion</td>
</tr>
<tr>
<td>2</td>
<td>Fig. 3B</td>
<td>AS</td>
<td>−10.0 ± 1.5</td>
<td>2.3 ± 0.8</td>
<td>−0.8 ± 0.2</td>
<td>3.2 ± 0.5</td>
<td>−4.0</td>
<td>Intorsion</td>
</tr>
<tr>
<td>3</td>
<td>Fig. 3C</td>
<td>0</td>
<td>8.6 ± 1.6</td>
<td>−1.0 ± 1.0</td>
<td>−2.4 ± 0.2</td>
<td>−1.6 ± 1.5</td>
<td>−0.8</td>
<td>Intorsion</td>
</tr>
<tr>
<td>4</td>
<td>Fig. 3D</td>
<td>OTR</td>
<td>10.6 ± 2.4</td>
<td>−6.7 ± 0.7</td>
<td>−5.3</td>
<td>−11.1</td>
<td>5.8</td>
<td>Extorsion</td>
</tr>
<tr>
<td>5</td>
<td>OP</td>
<td>AS</td>
<td>−6.1 ± 3.2</td>
<td>−3.0</td>
<td>−4.0</td>
<td>−1.6</td>
<td>−2.4</td>
<td>Intorsion</td>
</tr>
<tr>
<td>6</td>
<td>L pons</td>
<td>1.5</td>
<td>−12.9 ± 2.0</td>
<td>0.7 ± 0.7</td>
<td>−0.6 ± 0.7</td>
<td>1.8 ± 0.5</td>
<td>−2.4</td>
<td>Intorsion</td>
</tr>
<tr>
<td>7</td>
<td>R lateral medulla oblongata</td>
<td>OTR</td>
<td>15.2 ± 0.7</td>
<td>10.4 ± 0.8</td>
<td>11.4</td>
<td>8.9</td>
<td>2.6</td>
<td>Extorsion</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>OTR</td>
<td>8.5 ± 2.1</td>
<td>7.0 ± 2.9</td>
<td>6.7 ± 4.2</td>
<td>5.7 ± 2.3</td>
<td>1.0</td>
<td>Extorsion</td>
</tr>
<tr>
<td>9</td>
<td></td>
<td>OTR</td>
<td>5.9 ± 1.4</td>
<td>3.6 ± 1.5</td>
<td>5.6 ± 1.3</td>
<td>3.9 ± 1.1</td>
<td>1.7</td>
<td>Extorsion</td>
</tr>
<tr>
<td>10</td>
<td></td>
<td>0</td>
<td>0.1 ± 1.3</td>
<td>−2.1 ± 0.7</td>
<td>−1.8 ± 0.2</td>
<td>−2.1 ± 0.4</td>
<td>0.3</td>
<td>Extorsion</td>
</tr>
</tbody>
</table>

R = right; L = left; QP = quadrigeminal plate (indentation from pineal mass); AS = aqueduct syndrome; OTR = ocular tilt reaction.

Figure 7 (A) Right versus left eye roll results. Each datum point represents the mean of five measurements. (B) Right-left differences in roll versus deviations in pitch; data from Table 2. Positive differences represent extorsions, negative intorsions. Cases 8–10 have the same lesion as Case 7. Inset: least squares regressions and correlations squared.

Table 2 Eye signs, deviations in pitch and roll (means ± SD) and torsion categories in well-defined focal lesions

Visual upright in 3D
Brain 2010: 133; 3541–3551 | 3547
impairment. The reason why the classical abnormalities of vertical gaze associated with the aqueduct syndrome and PSP found little counterpart in deviations of the subjective vertical probably reflects dependencies on partly different neural substrates, namely, substrates involved in dynamic and static gaze control, respectively.

A somewhat clearer picture of directional dependencies emerged on analysis of cases with focal midbrain lesions where negative deviations appeared to be associated with dorsal locations and vice versa (Fig. 3). Additional support for this interpretation may be derived from the obstructive hydrocephalus and pineal groups, both of which had a clear preponderance of negative deviations, suggesting that the negative sign may relate to involvement of the midbrain tectum, by deformation and/or compression, in the dorsal direction in the hydrocephalic group and in the ventral direction in the pineal group. Clearly, these proposals require further study. Examination of additional cases with well-defined, minute lesions should be most informative in this regard. Unfortunately, such cases are rarely encountered. Larger lesions may simultaneously involve neural structures associated with positive and negative pitch. Figure 3 suggests a close apposition, at least in the upper midbrain. Meanwhile, in clinical settings, the mere finding of a deviation in pitch may help to alert to the likely presence of a structural lesion in otherwise unexplained instances of vertigo and impaired balance.

A noteworthy feature of most deviations arising in acute settings was their evanescent nature, with a more or less exponential tapering-off during subsequent days or weeks (Fig. 4). A similar time-course was observed after successful treatment of presumably long-standing obstructive hydrocephalus, using ventriculostomy or ventriculo-peritoneal shunting. However, deviations presumably existing for years have been observed in other hydrocephalic patients who had undergone repeated shunt revisions (and therefore failed to meet the present inclusion criteria). Similar observations have been made for deviations in roll; whether improvement is due to actual healing or to central compensation is not clear (Cnyrim et al., 2007).

Deviations in roll

There are several previous reports centred on focal brainstem disorders, as outlined in the 'Introduction' section. The present report confirms these previous results, although the overall prevalence of deviations was lower here. The difference may at least in part be due to the wider normal limits associated with clinical measurements. The prevalence was lower in the diffuse lesion group than in the focal one (Fig. 2B). As to the direction of deviation, strictly right-sided focal lesions tended to be associated with clockwise deviations and vice versa. The direction was not clearly predictable with median and paramedian lesions, suggesting the presence of crossings within the neural substrate.

Overall, deviations in roll were smaller and less frequent than deviations in pitch. The two measures were generally not correlated, although the ocular tilt reaction subgroup formed a striking exception (Fig. 6A and B). For another major subgroup, aqueduct syndromes, too few measurements were made in roll to allow any conclusion, and with other focal clinical constellations, e.g. internuclear ophthalmoplegia, too few instances meeting the inclusion criteria were observed. The high prevalence of ocular tilt reactions is attributable to a wide distribution of its neural substrate; the present ocular tilt reaction material comprised lesions involving the midbrain \((n = 1)\), pons \((n = 6)\), medulla \((n = 4)\) and cerebellum \((n = 1)\).

Combined deviations

Measuring deviations in roll has the advantage of simplicity; even a plain wastepaper basket will do. Assessment of deviations in pitch is somewhat more involved, requiring suitable equipment and a test space devoid of visual references. The test device described here (Fig. 1) can be fairly easily assembled from off the shelf components. An interesting alternative is to use a three-dimensional (3D) computer graphics display. A prototype employing the anaglyph technique to separate the right and left eye images is presently being tested in a personal computer setting; it allows simultaneous assessment of deviations in pitch and roll. The strong advantage of testing in both pitch and roll is the higher yield. Furthermore, whenever deviations in pitch and roll co-exist, a combined test can be held to be more natural than separate tests.

Combined deviations are quite common (Fig. 8), indicating that the true axis often deviates from traditional reference planes. This is not an unexpected finding. Consideration of the physical sizes of typical clinical lesions in relation to the dimensions and spatial distributions of the central vestibular and ocular motor networks suggests a strong potential for multi-planar manifestations. Such manifestations need not be restricted to ocular deviations. Indeed,
combined lateral and sagittal deviations have been documented with truncal lateropulsion in the Wallenberg syndrome (Dieterich and Brandt, 1992). Hence, subdivisions according to single, geometrically constructed planes appear inappropriate. Similarly, caution seems prudent when attempting to predict the deviation patterns of specific lesions; variation is considerable (Fig. 2 and Table 1).

The term ‘visual upright in 3D’ is suggested to identify unrestricted measurements, preserving the established term ‘visual vertical’ for measurements confined to the roll plane. In this context, mention should be made of a possible third aspect of deviation, namely, in the horizontal or yaw plane. The possible utility of assessing deviations in yaw with brainstem diseases remains to be explored. Although simple straight-ahead pointing tests have found use in neglect research (Richard et al., 2004), their accuracy may be debatable because of the difficulty in obtaining a physical reference. Using a laboratory test, Hamann et al. (2009) have recently documented deviations in yaw in patients with peripheral vestibular disease.

Incidentally, several previous investigations of deviations in roll have employed horizontal rather than vertical test targets. Horizontal targets provide little or no information as to position in pitch and would, on these grounds, appear to have a limited role in clinical diagnosis.

**Pathophysiological aspects**

Regarding the neural substrates of deviations, the roll deviations associated with ocular tilt reaction have been attributed to involvement of vestibulo-ocular neural pathways; for detailed overviews, see Brandt and Dieterich (1995), Brodsky et al. (2006), Baier et al. (2008) and Zwergal et al. (2009b). In brief, these graviceptive pathways carry otolith and semicircular canal signals via vestibular nuclei and vertical ocular motor control structures in the upper midbrain to the oculorotatory muscles; these signals are subjected to cerebellar modulation. A unilateral lesion causes asymmetry of resting tone in yoked pairs of oculorotatory muscles and results in cyclotorsion of the eyes. The torsion can be seen by ophthalmoscopy and documented by fundus photography. Surprisingly, objectively measured torsions and perceived deviations of the subjective visual vertical have been held to correlate poorly or not at all (Dieterich and Brandt, 1992, 1993a; Brandt and Dieterich, 1995; Brodsky et al., 2006). For example, Dieterich and Brandt (1992) presented detailed measurements from 14 subjects with Wallenberg syndrome, with correlation coefficients of 0.13 and 0.26 for ipsi- and contralateral eyes, respectively. The weak correlations were taken to imply a complex pathophysiology, where the primary fault was thought to involve a defective internal representation of the gravitational vertical, with secondary and mutually more or less independent torsions and deviations of the subjective visual vertical.

It can be argued that Dieterich and Brandt’s (1992) numerical data can be used more effectively, namely, to illuminate a specific hypothesis. The simplest hypothesis is that torsions and deviations are actually equal, except for stochastic variations. The hypothesis predicts that the application of a linear least squares regression with an origin constraint should return a direction coefficient near unity. Using the data from Dieterich and Brandt’s (1992) Fig. 4A and B, the analyses returned direction coefficients equaling 0.95 and 0.97, respectively, and correlation coefficients of 0.57 and 0.42. The relatively weak correlations appear to be well explained by the numerous sources of variation listed by the authors. In another material comprising 38 cases with a diversity of brainstem lesions, the regression over graphically measured mean torsions and perceived binocular deviations in roll returned regression and correlation coefficients of 0.98 and 0.77, respectively (L. Frisén, unpublished data). Recognizing the occasional occurrence of exceptional cases [e.g. one of those contained in Dieterich and Brandt’s (1992) Fig. 4], the hypothesis of a one-to-one relationship between measured torsions and subjective deviations in roll actually appears well supported for a large majority of brainstem lesions. Associations between torsion and deviations appear to be more loosely defined for presumed vestibular cortex lesions and lacking for anterior thalamic lesions (Dieterich and Brandt, 1993b; Brandt et al., 1994).

A detailed neuroanatomical model of deviations in pitch cannot be generated from the present material, but the close correlation between deviations in pitch and roll observed with ocular tilt reactions (Fig. 6B) points to common or juxtaposed substrates. However, the full set of observations points in the other direction, with virtually no correlation at all (Fig. 6A). The apparent contradiction may be resolved by attending to monocular measurements of deviations in roll. The following model is proposed to account for deviations in both pitch and roll with unilateral lesions.

The primary event is a lesion of the vestibulo-ocular neural substrate that results in cyclotorsion of one or both eyes. Although the torsions cause misalignments of the retinal images of the external world relative to accustomed retinal references, these retinal references can be subconsciously over-ridden by lifelong experience, e.g. the well-known verticality of door frames, to retain a normally oriented percept of the external world.

In the absence of external visual references to upright, reliance has to be made on accustomed retinal references, with perceptual uncovering of torsion and the generation of a corresponding deviation in roll in the test situation. However, depending on what component parts of the neural substrate are involved, left and right eye torsions may come out unequal, with unequal deviations in roll. Such inequalities are commonly encountered (Fig. 7) and are proposed to constitute the key cause of deviations in pitch. The reasoning may be best understood in terms of spatial geometry and with reference to an imaginary retinal vertical meridian. Consider a plane projected from the retinal vertical meridian into external space. With the introduction of some degree of convergence between the two eyes, the two planes, one from each eye, will intersect at the convergence point, producing an upright line of intersection (Fig. 9A). The addition of some torsion to both eyes will change the orientations of their meridional planes and also the orientation of the line of intersection. With symmetrical extorsions, the intersection line will acquire a positive deviation in pitch with its upper part projecting away from the point of convergence. The opposite deviation will occur with symmetrical intorsions (Fig. 9B and C). On the other hand, symmetrical, conjugate (same-direction) torsions will not generate appreciable deviations in pitch (Fig. 9D).
Validity of proposed model

The reasoning may appear foreign to real life situations, not least because of the lack of an anatomically defined retinal vertical meridian; however, the reasoning can easily be validated by self-observation, with the aid of so-called Dove prisms. These prisms have the unusual property of rotating the optical image on rotation of the prism. Hence, looking into a Dove prism that is being rotated around its long axis, the external world appears to roll around the line of sight. Because the field of view is flipped laterally, two prisms are needed, one in front of each eye, held in one hand each, with their base surfaces vertical. In the absence of prism rotation, the binocular view through the prisms is unremarkable except for the flipped laterality. However, on conjugate rotation of the prisms, the view-field will turn in the same direction, i.e. in roll. On symmetrical disjuge rotations of the prisms, the view-field will tilt in pitch instead. To see a combined deviation in pitch and roll, the prisms must be rotated to different degrees. Deviations are easiest to observe against a uniform background provided with a contrasting vertical line. An alternative technique is to use two Maddox rod lenses. A distant point light viewed through a Maddox lens is transformed into a bright line centred on the line of sight; rotation of the lens rotates the image. The view-field is otherwise blank, without visual cues to the orientation of the external world. In combination with a trial frame, dual Maddox lenses might furnish a useful clinical test for deviations in both roll and pitch, obviating the need of custom-built equipment and darkroom facilities.

Returning to the clinical situation and monocular testing, symmetrical disjuge torsions are expected to generate corresponding monocular deviations in roll. In binocular testing, on the other hand, the monocular deviations will cancel out to produce a normal binocular roll result, leaving a deviation in pitch only. Actually, symmetrical disjuge torsions are very rarely encountered; the vast majority of cases present with conjugate but asymmetrical roll (Fig. 7A). In principle, the degree of disjugation (the inter-ocular difference in roll) will still determine the perceived deviation in pitch, whereas the mean monocular roll will determine the perceived binocular deviation in roll. In reality, there will be considerable variation, even in cases with well-defined lesions (Fig. 7B). Part of the variation may be attributable to insufficient precision of measurements. Another contribution may come from co-existing rotatory nystagmus of small amplitude; this is common but difficult to recognize without the wide-angle view available to fundus photographers (L. Frisén, unpublished data). Additional sources of variation may derive from the operation of presently uncharted or unknown factors, including variations in convergence and deviations in yaw.

Perfectly symmetrical disjuge deviations in roll were not encountered in the present material. It may be speculated that such deviations should arise only with bilateral and perfectly symmetrical lesions. However, the present observation of normal binocular roll in three instances of the one-and-a-half syndrome, which comprises ipsilateral horizontal gaze paralysis and internuclear ophthalmoplegia (Wall and Wray, 1983), suggests that the vestibulo-ocular pathways occasionally may be affected bilaterally by a single paramedian lesion (here involving the pontine paramedian reticular formation and/or the abducens nucleus), located close to substrate crossings. Peculiarly, all three cases had substantial negative deviations in pitch. Previously, truly bilateral lesions have been proposed as mediators of both laterally alternating skew deviation and up- and down-beat nystagmus (Brandt and Dieterich, 1995; Brodsky et al., 2006). The state of the visual upright in 3D remains to be explored in these conditions.

Returning to the graphic model (Fig. 9), quantitative parameter variation revealed a nearly proportional relationship between inter-eye differences in torsion and deviations in pitch: a 1° difference produces ~3° of deviation. The roll-to-pitch gearing-up or magnification effect decreases with increasing viewing distance and increasing pupil separation; the 3× magnification just described applies to a viewing distance of 0.4 m and a pupil separation of 60 mm. The magnification effect may help to explain why deviations in pitch were more commonly observed than deviations in roll in the present material.

The proposed model predicts spurious relationships between inter-eye differences in roll and binocular deviations in roll; the correlation coefficient equalled 0.01 for well-localized lesions (Table 2). On the other hand, the model predicts a directly proportional relationship between inter-eye differences in roll and binocular deviations in pitch, with a direction coefficient larger than

Figure 9 Graphic perspective models of planes projected from each eye’s vertical meridian, with symmetrical convergence. (A) Normal state; (B) bilateral extorsions produce forward tilting of the line of intersection; (C) bilateral intorsions and backward tilting; (D) conjugate torsions produce tilt in roll only, not in pitch. Note that covering one eye should change the percept from a deviation in pitch to deviation in roll. Torsions were set to 10° and the convergence point was placed at three times the interpupillary distance. Models were generated in trueSpace 5 (www.caligari.com).
unity (because of the magnification effect). The regression and correlation coefficients equalled 2.71 and 0.82 ($P < 0.01$), respectively (Fig. 7B), indicating support for the model. Further, the model predicts that subjects who perceive deviations in pitch should experience a change in the percept into roll on occlusion of one eye. Spontaneous descriptions of such changes have been noted on several occasions but not collected systematically.

Anatomical proof for the model cannot currently be provided. Notably, a direct assessment of any deviation in pitch is not possible in the absence of normal binocular vision and stereopsis, e.g., in subjects suffering from strabismic amblyopia. An indirect assessment is still possible, however, by measuring monocular deviations in roll and calculating the inter-eye difference. The measurements need to be quite precise: a difference as small as 1.5° corresponds to a deviation in pitch of $\sim 4.5°$, which is just outside normal limits.

Assessment of the visual upright in 3D provides a new, quantitative angle on brainstem disorders. The test appears useful both for identifying a ubiquitous yet clinically silent feature of brainstem disease and for monitoring the evolution of underlying conditions. More detailed explorations appear well motivated.

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**References**


